UNIVERSIDAD POLITÉCNICA DE VALENCIA

# Genetic Analyses of Reproductive Traits in Maternal Lines of Rabbits and in their Diallel Cross

## Análisis Genético de Caracteres Reproductivos en Líneas Maternales de Conejo y en su Cruzamiento Dialélico

**Ph.D. Thesis**

**Mohamed M. Ragab Ghanem**

Under supervision of:
**Prof. Dr. Manuel Baselga Izquierdo**
Valencia, May 2012

# Genetic analyses of reproductive traits in maternal lines of rabbits and in their diallel cross

This Thesis has been submitted in fulfilment of the requirements for the degree of Doctor of Science at the Universidad Politécnica de Valencia.

By

**Mohamed M. Ragab Ghanem**

Thesis supervisor

**Prof. Dr. Manuel Baselga Izquierdo**
Instituto de Ciencia y Tecnología Animal
Universidad Politécnica de Valencia

The most perfect believers are those who are best in attitude

Love for the other People what you love for yourself

**The Prophet Muhammad (محمد رسول الله)**

# *DEDICATION*

*I dedicate this work to whom my heartfelt thanks; to my parents, wife and son for their patience and help. These times have been very hard for you and for me. Thank you for your strength and support, for your understanding and your love.*

*As well as to my friends for all the support they lovely offered along the period of my post-graduation.*

# ACKNOWLEDGEMENT

*Thanks to My god (ALLAH)*

Firstly, I am gratefulto my family (My beloved father and mother, my lovely wife (**Asmaa**) and my son (**Youssof**) for their continuous support, help and creditable encouragement.

I'd like to express my deep and sincere gratitude to my supervisor, **Manuel Baselga**, that his wide knowledge and reasonable thinking ways were awfully valuable for me. Also, His understanding, encouraging and personal guidance have provided a good basis for the present thesis. For me, he is more than supervisor. Manolo, thanks for placing your trust in me.

My extremegratefulnessto my colleagues, with special affection to: **Agustín Blasco**, for his preciousadvice, help, critical revision of this manuscript, extensive discussions around my work and interesting comments have been very helpful for this study; **Maria Antónia Santacreu,** for her sharing me the scientific ideas, advices, encouragement and support during this work; **Jose Vicente**, for his help and qualifiedme for Laparoscopy; **Rosa** and **Pilar**, for thier encouraging and support.

My special thanks to my friend **Juan Pablo Sanchez** (my brother), for his guidance in statistical analysis, encouraging and essential assistance in reviewing this study. Also, I wish to thank **Llibertat** (my daughter), for his help when I came to Spain without Spanish, and continued so far. On the other note my thanks to my friend **Sofian,** for their encouragement and their Permanent contact with me.

During this work I have collaborated with colleagues for whom I have great regard, and I wish to extend my warmest thanks to all those who have helped me specially my friends **Carlos** and **Cefe Torres** who travelled with me to the farms to do high number of laparoscopy operations (2050 does).

My sincere thanks are due to the official referee, **Miriam Piles, Juan Pablo Gutiérrez** and **Luis Varona,** for their detailed review, constructive criticism and excellent advice during thesis preparation

I am deeply grateful to all members of the Department of Animal science, Universidad Politécnica de Valencia, with special affection to my friends in the fourth floor, **Criz, Vero** and **Pati**for sharing our joys, problems and doubts.I did not feel with them that I am in a foreign country during 4 years. Thank you so much.

Also, my thank to members of animal Farm **(Rafa, Ion** and **Noelia)**, for their continuous help, encouragement and friendship.My research would not have been possible without their helps.

My eternal thanks to: **Ahmed Yehia** who helped me in formatting the thesis to be in a good state and provided me the time without limit**;** **Ayman El Nagar** and **Ayman Saeed**for their help and encouragement.

My sincere thanks to my Egyptian friends: **Tarek,** with his friendship during the 4 years enabled him to be as a brother to me; **M. Ali**, he was a good friend and he always gave me right advices; **M. Maher**, **Abd Allah**, **Sameh**, **M. Alaa** and **Abeer** for their supporting, encouraged and for the good time we shared in Valencia.It would have been a lonely life without them.

I'm most grateful to the **Colegio Mayor la Coma**, especially: the director **Alfonso García** and sub director **Jorge Amaya** and **Reinaldo Fajardo**, for there supporting, advices and helped me to exchange powerful scientific ideas and cultures with persons from different countries and upgrade my personality

Many Thanks to my friends from Algeria (**Zoulikha**), Tunisia (**Chiraz**, **Abd El Hadi**, **Nidal**, **Walid** and **Wadii**) and Morocco (**Youssof** and **Amal**), for their continuous encouragement and sharing a good time.

My sincere thanks also go to **Kamal Saleh**, professor of poultry breeding and genetics, Kafr El Sheikh University, Egypt, for his motivation and enthusiasm. His guidance helped me in my personality formation and solving many problems in all the time of my career.

Many thanks are due to the staff of Poultry Production Departament, Kafr El Sheikh University, Egypt, for their continuous encouragement and allow me to travel to get a doctorate from Spain to prepare me as a scientist.

Fainlly, special acknowledgement is due to the Spanish Research Projects (**CICYT**) **AGL2008-03274**, **ACOMP09 /013** (Valencian Generality, Spain) and Spanish Research Projects (**MEC-CICYT**) **AGL2011-30170-C02-01** for granting and supporting this work to prepare me as a scientist.

*Thanks for all*

*Gracias a Todos*

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## Abstract

The general aim of this thesis has been to evaluate the productive performance of four maternal lines of rabbits as well as their corresponding crossbreds, and in addition to estimate the crossbreeding genetic parameters, from a complete diallel cross.The lines were A, V, H and LP,founded on different criteria but all of them selected for litter size at weaning since their foundation until present, for 41, 37, 20 and 7 generations, respectively.

In chapter 3**,** comparison between lines was made at the foundation time of the lines, using mixed animal models including additive and permanent random effects. In this analysis all the process of selectionwas considered by including the complete data set (recorded from June 1980 to February 2009) and the full pedigree. A second comparison was made at fixed times when does from different lines were bred in the same farm and under the same feeding and management conditions: i) from March 1997 to August 1998, for lines A, V and H, and ii) from September 2007 to February 2009 for lines A, V and LP. The models used for these second analyses did not include the additive genetic effects and only consider the records of each period; therefore line comparisons were not dependent on the genetic model.The raw means for 47,132 parities produced from 12,639 does were 9.80, 9.07, 7.79 and 6.95 rabbits for total born, number born alive, number weaned and number marketed per litter, respectively, and 49.80 days for kindling interval, demonstrating high levels of productivity of these lines. At their respective times of foundation, line A showed the lowest litter size, being important the difference between this line and the average of the other lines: 1.39 rabbits per litter for total born, 1.20 for number born alive, 0.84 for number weaned and

1.06 for number marketed. Lines V and H did not show significant differences for litter size traits, but for kindling interval the contrast was 3.30±0.72d, which was significant and favourable to line H. LP line exceeded V line by approximately one rabbit for all litter size traits. The differences between these lines for kindling interval were negligible. Some interactions between lines and farm-year-seasons were important. Regarding the comparison of lines A, V and H from March 1997 to August 1998, the pattern of the differences between the line A and the others was similar to those observed at the origin, and the only significant difference between lines V and H was found for the kindling interval (4.62 d in favour of line V) . The comparison between the lines A, V and LP from September 2007 to February 2009 indicates that differences in reproductive performance between lines were lower than at the origin. In general, good agreement was observed between the comparisons of lines for litter size traits at fixed times, using a model without genetic effects and data recorded during the comparison periods, and the predictions derived from the model with genetic effects and the complete data set.. Another point is the importance of the criteria used in each line to select the founders in determining the initial performance levels.

The aim of chapter 4 was to use demographic and litter size data of the previous lines, as a case study, in order to: i) estimate their effective population size, in order to monitor the rate of increase of inbreeding with selection and ii) study whether the inbreeding effect on litter size traits depends on the pattern of its accumulation over time. The lines were kept closed at the same nucleus of selection under the same program of selection and management. Some practices in mating and selection management, such as avoiding matings between animals sharing grandparents and making that each sire contributed with a son to the next generation,allowed an increase of the inbreeding coefficient lower than 0.01 per generation in these lines of around 25 males and 125 females. The effective population size (Ne) for them was around 57.3, showing that the effect of selection on increasing inbreeding, has been counterbalanced by the management practices which try to reduce

increase of inbreeding. The inbreeding of each individual was partitioned in three components: old inbreeding (inbreeding accumulated between the foundation of the line and generation 15th for animals born after generation 30th), intermediate (inbreeding accumulated between generations 15th to 30th for animals born after generation 30th or the inbreeding accumulated in the first 15generation for animals born before generation 30th) and new (the rest of situations). The coefficients of regression of the old, intermediate and new inbreeding on total born (TB), number born alive (NBA) and number weaned (NW) per litter, showed a decreasing trend from positive to negative values. Regression coefficients significantly different from zero were those for the old inbreeding on TB (6.79±2.37) and BA (5.92±2.37). The contrast between the regression coefficients associated to old and new inbreeding were significant for the three litter size traits: 7.57±1.72 for TB; 6.66±1.73 for BA and 5.13±1.67 for NW. These results have been interpreted as the combined action of purging of unfavourable aleles and artificial selection against these aleles which was favoured by inbreeding along generations of selection through the increase of homozygotes frequency.

The previous maternal rabbit lines were used in a complete diallel cross to produce sixteen genetic groups (four maternal lines and twelve single crosses). The objective of this experiment was to evaluate reproductive traits and functional longevity of crossbred and purebred does. The sixteen genetic groups were distributed in four Spanish farms but only one genetic group (V line) was present in all farms to connect records among these farms and to be used as the reference genetic group. The records of these traits were obtained from January 2009 to October 2011. The differences between all genetic groups and V line were estimated. Then, direct and maternal genetic effects of the lines, and direct heterosis between the lines were estimated according to Dickerson's model.

Chapter 5, aimed to study ovulation rate **(OR),** number of implanted embryos **(IE),** total born **(TB),** embryo survival **(ES),** fetal survival **(FS)** and prenatal survival **(PS).** An animal model was used.The means for all traits

were higher than the ones obtained in previous studies in these lines. Differences in OR and IE between lines were not significant despite A line showed relevant lower OR than the other lines, whereas the differences were significant and relevant for TB. Regarding the differences between the crossbred groups and V line, only significant differences were observed in favour of HxV. In general, the positive effect of crossbreeding on IE is primarily due to the lower pre-implantation loss and the observed differences were not significant. Regarding TB, the obtained differences were important in two cases: favourable in the case of AxH and unfavourable in the case of LPxV. In general, relevant but no always significant differences between lines in direct genetic effects were found although the magnitude of the differences was high for some traits. Line LP presented larger direct genetic effects than any other line, being significantly different to line A.Differences in maternal effects were not significant, except those between the LP and V lines. High and positive heterosis effect was found between lines A and H. The cross between lines LP and V had a negative heterosis for all traits with a highly negative effect on TB (16% of the mean).

In Chapter 6, litter size (total born **(TB)**, number born alive **(NBA)** and number weaned **(NW)**) and kindling interval **(KI)** were analyzed with the aim to get estimates of crossbreding genetic parameters. Only, LP line presented a higher direct genetic effect than V line being significant the effect on NBA. Between the other lines no significant differences in direct and maternal genetic effects for TB, NBA and NW were found but there were significant differences for KI. A relevant and large heterosis effect was found for TB in the cross HxV, this parameter for the crosses AxH, AxV and LPxH was lower. For NBA, significant heterosis was found in HxV and AxV and for NW in AxV, LPxH and LPxV. Favourable and significant heterosis for KI was found in AxV and LPxV, whereas in AxLP and LPxH the heterosis was unfavourable and significant. Crossbred does, generally, showed a higher reproductive level than V females and the differences between the average of all crosses andline V were important, being 0.45 for TB, 0.57 for NBA, 0.75 for NW and -2.22 d for

KI.The contrast between every two lines showed a similar performance of the lines and we did not find significant differences among them for litter size. For KI, significant differences with relevant values were found between lines and it reflected the significant differences between direct and maternal genetic effects.

Last chapter of this thesis has aimed to study the functional longevity, defined as the number of days between the first positive palpation and the death or culling of the doe for reasons other than production; it represents the ability to delay involuntary culling. Records from 7,211 does were analysed with the Survival kit 6.0 using a Cox proportional hazard model of fixed effects. The model incorporated time-dependent factors, such as group-farm-year-season (GFYS), number born alive (NBA), group-order of positive palpation (GPPO) and physiological status of the female (PS).Lines A, H and V had a similar ability to avoid culling or death and they show higher risk of being culled of dead than LP line. Line LP had the lowest associated hazard with important differences at later ages and the probabilities to be replaced were 0.39, 0.49 and 0.53 times the replacement rate of lines A, H and V, respectively. We did not find significant differences between all crossbred groups and line V except for the cross between A and H lines in favour of line V.The difference between a cross and its reciprocal, generally, was not significant except between VxH and HxV, favourable to HxV and between LPxH and HxLP, in favour of HxLP. Line V had the highest associated risk due to the direct genetic effects and these differences were significant with respect to those for lines H and LP. The differences in maternal genetic effects were small and not significant except between lines H and V, favouring V line. The estimated heterotic effects do not follow the same direction but they showed, in some cases, the importance of the crosses between specialized lines to produce crossbred does for intensive meat rabbit production. Thus, it was shown that at the early productive cycles, the risk associated to purebreds was higher than the risk of crossbreds, when the cost of the does has not been recovered yet.

The contrary happened at late productive cycles (fifth cycle or more), when the cost of the does was already recovered.

There are some crosses that could be specially recommended to be used in commercial production like HxLP, HxV and AxV or VxA. Some of these recommendations took into account the fact that in commercial production the fostering after birth is a common practice. This fact gives an added value to crosses with high average TB or NBA but having lower performances for NW. The AxH cross could be recommended for farms where the longevity is not a problem.

# Resumen

El objetivo principal de esta tesis ha sido evaluar el rendimiento reproductivo de cuatro líneas maternales de conejos, de sus correspondientes cruces y la estima de los parámetros genéticos del cruzamiento, a partir de un cruce dialélico completo. Las líneas involucradas fueron la A, V, H y LP, fundadas bajo diferentes criterios pero, todas ellas, seleccionadas desde su origen hasta la actualidad por tamaño de camada al destete. Estas líneas se encuentran actualmente en la generación 41, 37, 20 y 7, respectivamente.

En el tercer capítulo, la comparación entre las líneas se hizo en la fundación de las mismas, usando un modelo animal mixto que incluía los efectos aleatorios aditivos y permanentes. Para realizar este análisis se consideró el proceso de selección, ya que se incluyó el conjunto completo de datos (recogidos desde junio de 1980 hasta febrero de 2009) y el pedigrí integro. La segunda comparación se realizó en un tiempo fijo, los últimos dieciocho meses en los las hembras de tres líneas diferentes compartieron la misma granja y estuvieron bajo las mismas condiciones de manejo y alimentación. Estos periodos correspondieron a los intervalos que van: i) Desde marzo de 1997 hasta agosto de 1998 para las líneas A, V y H, y ii) Desde septiembre de 2007 hasta febrero de 2009 para las líneas A, V y LP. Los modelos utilizados para estos análisis no incluyeron el efecto genético aditivo y solo se consideraron los datos provenientes de dichos periodos, por consiguiente, las comparaciones entre las líneas no dependieron del modelo genético. Las medias por camada, de los 47,132 partos producidos por las 12,639 conejas involucradas en este estudio, fueron de 9.8, 9.07, 7.79 y 6.95 para número total de gazapos nacidos, número de nacidos vivos, número de destetados y número de sacrificados,

respectivamente, y un intervalo entre partos de 49.80 días. Se puede observar como estas líneas tienen altos niveles productivos. En los respectivos momentos de fundación, la línea A mostró el menor tamaño de camada, siendo importante las diferencias con las medias combinadas de las otras líneas: 1.39 gazapos/camada para el total de nacidos, 1.2 para el número de nacidos vivos, 0.84 para el número de destetados y 1.06 para el número de sacrificados. Las líneas V y H no mostraron diferencias significativas para los caracteres de tamaño de camada, pero para el intervalo entre partos, el contraste fue 3.30±0.72días, que resultó significativo a favor de la línea H. La línea LP superó a la V en aproximadamente un gazapo para todos los caracteres de tamaño de camada estudiados. Las diferencias entre estas líneas para el intervalo entre partos fueron despreciables. Algunas interacciones, como la interacción entre línea y granja-año-estación resultaron importantes. Con respecto a la comparación entre las líneas A, V y H en el periodo que va desde marzo de 1997 hasta agosto de 1998, el patrón de las diferencias entre la línea A y las demás fue similar al observado en la fundación, y sólo se encontraron diferencias significativas entre las líneas V y H para el intervalo entre partos (4.62 días a favor de la línea V). La comparación entre las líneas A, V y LP, desde septiembre de 2007 hasta febrero de 2009 mostró una aproximación en sus rendimientos reproductivos, si son comparados con las diferencias que existían en el origen. De forma general, en la comparación de las líneas para los caracteres de tamaño de camada se observó una gran similitud en los periodos de tiempo fijo, usando un modelo sin efectos genético y datos recogidos durante los periodos de comparación, y las predicciones derivadas de los modelos con efectos genéticos. Otro punto a tener en cuenta, es la importancia del criterio utilizado para seleccionar los animales fundadores de cada línea, ya que determinarán los niveles iniciales de estos rendimientos reproductivos.

El objetivo principal del capítulo 4 fue usar los datos genealógicos y de tamaño de camada de las líneas anteriormente mencionadas para: i) estimar sus tamaños de población efectiva, como una medida del incremento de la tasa consanguinidad y ii) estudiar si el efecto de la consanguinidad en los caracteres

de tamaño de camada dependen del patrón de acumulación en el tiempo. Las líneas se han mantenido cerradas, en el mismo núcleo de selección, siguiendo el mismo manejo y programa de selección. Algunas prácticas, en lo correspondiente al apareamiento yla selección de los animales, como pueda ser evitar apareamientos entre animales con abuelos comunes y hacer que cada macho contribuya con un hijo a la siguiente generación, han permitido un incremento del coeficiente de consanguinidad menor de 0.01 por generación en estas líneas, cuyo tamaño, por generación, es alrededor de 25 machos y 125 hembras cada una. El tamaño efectivo de la población (Ne) para estas líneas estuvo entorno a 57.3, mostrando que el efecto de la selección, que produce un incremento de laconsanguinidad, ha sido en parte contrarrestado por el manejo empleado. La consanguinidad de cada individuo fue dividida en tres componentes: consanguinidad vieja (consanguinidad acumulada entre la fundación de la línea y la generación 15ª para los animales nacidos después de la generación 30ª), intermedia (consanguinidad acumulada entre las generaciones 15ª a la 30ª para animales nacidos después de la generación 30ª o la consanguinidad acumulada en las primeras 15 generaciones para los animales nacidos antes de la generación 30ª) y nueva (las demás situaciones). Los coeficientes de regresión de la consanguinidad vieja, intermedia y nueva, por camada, en el número total de nacidos (TB), número de nacidos vivos (NBA) y número de destetados (NW), mostraron una tendencia decreciente desde valores positivos hasta valores negativos. Los coeficientes de regresión significativamente diferentes de cero fueron los de la consanguinidad vieja en TB (6.79±2.37) y NBA (5.92±2.37). El contraste de los coeficientes de regresión entre la consanguinidad vieja y la nueva fue significativo para los tres caracteres de tamaño de camada: 7.57±1.72 para TB; 6.66±1.73 paraNBA y 5.13±1.67 para NW. Estos resultados se han interpretado como la acción combinada de la purga de genes desfavorables y de la selección artificial, favorecida por la consanguinidad a lo largo de generaciones de selección a través del incremento de homocigotos.

Las líneas maternales de conejo utilizadas en esta tesis, fueron utilizadas para generar un cruzamiento dialélico completo. Así, se generaron dieciséis grupos genéticos (cuatro líneas maternales y doce cruces simples). El objetivo de este experimento fue evaluar los caracteres reproductivos y la longevidad funcional de las hembras cruzadas y de las líneas puras. Los dieciséis grupos genéticos fueron distribuidos en cuatro granjas españolas, pero solo un grupo genético (línea V) estuvo presente en todas las granjas para conectar los datos entre estas y ser utilizada como grupo genético de referencia. Los datos de los caracteres reproductivos se obtuvieron desde septiembre de 2008 hasta el final de septiembre de 2011. Se estimaron las diferencias entre todos los grupos genéticos y la línea V. Así, las diferencias entre líneas para los efectos genéticos directos y maternos, y para el heterosis directa, se estimaron de acuerdo con el modelo de Dickerson.

En lo concerniente a los componentes de tamaño de camada, en conejoy en otras especies ganaderas, se han realizado pocos estudios previos que pretendiesen estudiar los efectos del cruzamiento. El capítulo 5, se dedicó a estudiar la tasa de ovulación (OR), número de embriones implantados (EI), número total de nacidos (TB), número de nacidos vivos (NBA), supervivencia embrionaria (ES), supervivencia fetal (FS) y supervivencia prenatal (PS). Se utilizó un modelo animal. Las medias para todos los caracteres fueron mayores que las que se habían obtenido en estudios previos de estas mismas líneas. Las diferencias encontradas en OR y IE entre las líneas no resultaron significativas, a pesar que para la línea A los valores de OR resultaron menores y relevantes en comparación con las otras líneas. Por otra parte, las diferencias fueron significativas y relevantes para TB y NBA. En lo referente a las diferencias entre los diferentes cruces y la línea V, sólo se hallaron diferencias significativas a favor del cruce HxV. De forma general, el efecto positivo del cruzamiento en IE es debido principalmente a las menores pérdidas pre-implantacionales y las diferencias observadas no fueron suficientes para resultar significativas. En cuanto a TB y NBA, las diferencias obtenidas fueron importantes en dos casos: favorable en el caso de AxH y desfavorable para el caso de LPxV. En general, se encontraron diferencias relevantes, pero no siempre significativas, entre las líneas en los efectos genéticos directos. La línea LP presentó los mayores efectos genéticos directos con respecto a las otras líneas, siendo significativamente diferente en relación con la línea A. Las diferencias en los efectos maternos fueron no significativas, exceptuando las encontradas entre las líneas LP y V. Entre las líneas A y Hse encontró un efecto de heterosis grande y positivo. El cruce entre las líneas LP y V tuvo una heterosis negativa para todos los caracteres, con un efecto muy negativo en TB y NBA (16% y 11% de media respectivamente).

En el capítulo 6, el objetivo fue analizar el tamaño de camada (nacidos totales (TB), número de nacidos vivos (NBA), número de destetados (NW) e intervalo entre partos (KI)). Solo la línea LP presentó un mayor efecto genético directo que la línea V, con un resultado significativo para NBA. Las otras líneas no mostraron diferencias significativas en los efectos genéticos directos y maternos para TB, NBA y NW pero hubo diferencias significativas para KI. Se estimó una heterosis grande y relevante para TB en el cruce HxV, seguido por los cruces AxH, AxV y LPxV. También se encontró una heterosis favorable y significativa para KI en los cruces AxV y LPxV, mientras que para los cruces AxLP y LPxH la heterosis fue significativa y desfavorable. Las conejas cruzadas, generalmente, mostraron un mayor nivel reproductivo en comparación con la línea V. Las diferencia entre la media conjunta de los cruces comparada con la línea V resultó importante, siendo 0.45 para TB, 0.57 para NBA, 0.75 para NW y -2.22 díaspara KI. El contraste entre cada dos líneas mostró un rendimiento similar y no encontramos diferencias significativas entre los efectos genéticos directos y maternos.

El último capítulo de esta tesis tuvo como objetivo estudiar la longevidad funcional, definida como el número de días entre la primera palpación positiva y la muerte o eliminación de la coneja por razones ajenas a la producción. De este modo, la longevidad funcional representa la capacidad del animal para retrasar su eliminación involuntaria. Se analizaron los datos de 7,211 conejas mediante el Survival Kit 6.0, utilizando un modelo de Cox de efectos fijos y riesgos proporcionales. El modelo incorporó factores dependientes del tiempo, como el grupo-granja-año-estación (GFYS), el número de nacidos vivos (NBA), grupo-orden de palpación positiva (GPPO) y estado fisiológico de la hembra (PS). Las líneas A, H y V tuvieron una capacidad similar para evitar la eliminación, siendo más sensibles que la línea LP. La línea LP tuvo el menor riesgo asociado, con diferencias importantes a edades tardías y una probabilidad de ser reemplazada de 0.39, 0.49 y 0.53 veces latasa desustituciónde las líneas A, H, y V. No encontramos diferencias significativas entre los diferentes cruces y la línea V, excepto con el cruce entre AxH a favor de línea V. Las diferencias entre un cruce y su reciproco, generalmente, no fue significativa, excepto entre los cruces VxH y HxV, favorable a la HxV, y para los cruces LPxH y HxLP, a favor del HxLP. La línea V tuvo el mayor riesgo asociado debido a los efectos genéticos directos y estas diferencias fueron significativas con respecto a las líneas H y LP. Por otra parte, las diferencias en los efectos genéticos maternos fueron pequeños y no significativos, excepto en las líneas H y V, siendo favorables a la línea V. La estima de los efectos de heterosis no sigue la misma dirección pero mostraron, en algunos casos, la importancia de los cruces entre líneas especializadas para producir conejas cruzadas para la producción intensiva de conejos de carne. Así, se observó que en ciclos productivos tempranos, el riesgo asociado a las líneas puras es mayor que el riesgo asociado a los diferentes cruces, siendo este el periodo en el quetodavía no se ha amortizado el coste de la coneja. Justamente lo contrario ocurre en ciclos productivos tardíos (5º ciclo o más), cuando el coste de la hembra ya ha sido amortizado.

Algunos cruces como HxLP, HxV, AxV o VxA pueden ser especialmente recomendados para su uso en granjas comerciales. Parte de estas recomendaciones tienen en cuenta el hecho de que la adopción de gazapos después del nacimiento, hecho que valoriza los cruzamientos en que es alto el número de nacidos totales o nacidos vivos, pero no lo estanto el número de destetados. También, el cruce AxH puede ser recomendado en granjas en las que los problemas de longevidad sean pequeños.

# Resum

L'objectiu principal d'aquesta tesi ha sigut avaluar el rendiment reproductiu de quatre línies maternals de conills, dels seus corresponents creuaments i l'estima dels paràmetres genètics del creuament, a partir d'un encreuament dialelic complet. Les línies involucrades foren la A, V, H i LP, fundades baix diferents criteris però, totes elles, seleccionades des del seu origen fins a l'actualitat per tamany de ventrada al deslletament. Estes línies es troben actualment en la generació 41, 37, 20 i 7 respectivament.

Al tercer capítol, la comparació entre les línies es va fer a la fundació de les mateixes, utilitzant un model animal mixt que incloïa els efectes aleatoris aditius i permanents. Per a realitzar aquest anàlisi es va considerar el procés de selecció, ja que es va incloure el conjunt complet de dades (arreplegats des de juny del 1980 fins a febrer del 2009) i el pedigrí íntegre. La segona comparació es va realitzar a temps fix, quan les femelles de les diferents línies van compartir la mateixa granja i van estar davall les mateixes condicions de maneig i alimentació. Aquestos períodes corresponen als intervals que van: i) Des de març de 1997 fins agost de 1998 per a les línies A, V i H, i ii) Des de setembre del 2007 fins a febrer del 2009 per a les línies A, V i LP. Els models utilitzats per aquest anàlisis no van incloure l'efecte genètic aditiu i només es van considerar les dades provinents dels períodes, per tant, les comparacions entre les línies no van dependre del model genètic. Les mitjanes, per ventrada dels 47,132 parts produïts per les 12,639 conilles involucrades en aquest estudi, foren de 9.8, 9.07, 7.79 i 6.95 per a nombre de catxaps nascuts, nombre de nascuts vius, nombre de deslletats i nombre de sacrificats, respectivament, i un interval entre parts de 49.80 dies. Es pot observar com estes línies tenen alts nivells productius. Als respectius moments de fundació, la línia A va mostrar el menor

tamany de ventrada, sent important les diferències amb les mitjanes combinades de les altres línies: 1.39 catxaps/ventrada per al total de nascuts, 1.2 per alnombre de nascuts vius, 0.84 per al nombre de deslletats i 1.06 per al nombre de sacrificats. Les línies V i H no van mostrar diferencies significatives per als caràcters de tamany de ventrada, però per a l' interval entre parts, el contrast va ser 3.30±0.72 dies, que va resultar significatiu a favor de la línia H. La línia LP va superar a la V en aproximadament un catxap per a tots els caràcters de tamany de ventrada estudiats. Les diferències entre estes línies per a l' interval entre parts van ser menyspreables. Algunes interaccions, com entre línies i granja-any-estació van resultar importants. Respecte a la comparació entre les línies A, V i H al període que va des de març de 1997 fins agost de 1998, el patró de les diferències entre la línia A i les altres va ser semblant a l'observat en la fundació, i només es van trobar diferències significatives entre les línies V i H per a l'interval entre parts (4.62 dies a favor de la línia V). La comparació entre les línies A, V i LP, des de setembre del 2007 fins a febrer del 2009 va mostrar una aproximació als seus rendiments reproductius, si es comparen amb les diferències que existien a l'origen. De forma general, a la comparació de les línies per als caràcters de tamany de ventrada es va observar una gran similitud als períodes de temps fix, usant un model sense efectes genètics i dades arreplegades durant els períodes de comparació, i les prediccions derivades dels models amb efectes genètics. Un altre punt a tindre en compte, és la importància del criteri utilitzat per a seleccionar els animals fundadors de cada línia, ja que determinen els nivells inicials d'aquestos rendiments reproductius.

L'objectiu principal del capítol 4va ser usar les dades demogràfiques i de tamany de ventrada de les línies anteriorment mencionades per a: i) estimar els seus tamanys de població efectiva, com una mesura de l'increment de la taxa consanguinitat i ii) estudiar si l'efecte de la consanguinitat en els caràcters de tamany de ventrada depenen del model d'acumulació en el temps. Les línies s'han mantingut tancades, en el mateix nucli de selecció, seguint el mateix maneig i programa de selecció. Algunes pràctiques, en lo corresponent a l'aparellament i la selecció dels animals, com puga ser evitar aparellaments entre animals amb iaios comuns i fer que cada mascle contribuïsca amb un fill a la següent generació, han permés un increment del coeficient de consanguinitat menor de 0.01 per generació en estes línies, que compten amb uns 25 mascles i 125 femelles cada una. El tamany efectiu de la població (NE) per a estes línies va estar entorn a 57.3, mostrant que l'efecte de la selecció, que produïx un increment de la consanguinitat, ha sigut contrarestat pel maneig emprat, que ha intentat reduir d'increment de la dita taxa. La consanguinitat de cada individu va ser dividida en tres components: consanguinitat vella (consanguinitat acumulada entre la fundació de la línia i la generació 15a per animals nascuts després de la generació 30a), intermèdia (consanguinitat acumulada entre les generacions 15a a la 30a per animals nascuts després de la generació 30a o la consanguinitat acumulada en les primeres 15 generacions per animals nascuts després de la generació 30a) i nova (les altres situacions). Els coeficients de regressió de la consanguinitat vella, intermèdia i nova, per ventrada, en el nombre total de nascuts (TB), nombre de nascuts vius (NBA) i nombre de deslletats (NW), van mostrar una tendència decreixent des de valors positius fins valors negatius. Els coeficients de regressió significativament diferents de zero van ser els de la consanguinitat vella en TB (6.79±2.37) i NBA (5.92±2.37). El contrast dels coeficients de regressió entre la consanguinitat vella i la nova va ser significatiu per als tres caràcters de tamany de ventrada: 7.57±1.72 per a TB; 6.66±1.73 per a NBA i 5.13±1.67 per a NW. Estos resultats s'han interpretat com l'acció combinada de la porga de gens desfavorables i de la selecció artificial, afavorida per la consanguinitat al llarg de generacions de selecció a través de l'increment d'homocigotos.

Les línies maternals de conill citades anteriorment, van ser utilitzades per a generar creuaments dialelics complets. Així, es van generar setze grups genètics (quatre línies maternals i dotze encreuaments simples). L'objectiu d'aquest experiment va ser avaluar els caràcters reproductius i la longevitat funcional de les femelles creuades i de les línies pures. Els setze grups genètics van ser distribuïts en quatre granges espanyoles, però només un grup genètic (línia V) va estar present en totes les granges per a connectar les dades entre estes i ser utilitzada com a grup genètic de referència. Les dades dels caràcters reproductius es van obtindre des de setembre del 2008 fins al final de setembre del 2011. Es van estimar les diferències entre tots els grups genètics i la línia V. Així, les diferències entre línies, els efectes genètics directes i materns, i heterosis directa entre les línies, es van estimar d'acord amb el model de Dickerson.

Pel que fa als components de tamany de ventrada en conill, s'han realitzat pocs estudis previs i en altres espècies ramaderes es van fer a fi d'estudiar els efectes del encreuament. El capítol 5, es va dedicar a estudiar la taxa d'ovulació (OR), nombre d'embrions implantats (EI), nombre total de nascuts (TB), nombre de nascuts vius (NBA), supervivència embrionària (ÉS), supervivència fetal (FS) i supervivència prenatal (PS). Es va utilitzar un model animal. Les mitjanes per a tots els caràcters van ser majors que les que s'havien obtingut en estudis previs d'aquestes mateixes línies. Les diferències trobades en OR i IE entre les línies no van resultar significatives, a pesar que per a la línia A els valors de OR van resultar menors i rellevants en comparació amb les altres línies. D'altra banda, les diferències van ser significatives i rellevants per a TB i NBA. Pel que fa a les diferències entre els diferents encreuaments i la línia V, només es van trobar diferències significatives a favor de l'encreuament HxV. De forma general, l'efecte positiu del encreuament als IE és degut principalment a les menors pèrdues pre-implantacionals i les diferències observades no van ser suficients per a resultar significatives. En quant a TB i NBA, les diferències obtingudes van ser importants en dos casos: favorable en el cas de AxH i desfavorable per al cas de LPxV. En general, es van trobar diferències rellevants, però no sempre significatives, entre les línies als efectes genètics directes, encara que la magnitud de les diferències va ser gran per a alguns dels caràcters. La línia LP va presentar els majors efectes genètics directes respecte a les altres línies, sent significativament diferent en relació amb la línia A. Les diferències en les efectes materns van ser no significatives, exceptuant les trobades entre les línies LP i V. Un efecte d'heterosis, gran i positiu, es va trobar entre les línies A i H. L'encreuament entre les línies LP i V va tindre una heterosis negativa per a tots els caràcters amb un efecte gran i negatiu a TB i NBA (16% i 11% de mitjana respectivament).

En el capítol 6, l'objectiu va ser analitzar el tamany de ventrada (nascuts totals (TB), nombre de nascuts vius (NBA), nombre de deslletats (NW) i interval entre parts (KI)). Només la línia LP va presentar un major efecte genètic directe que la línia V, amb un resultat significatiu per a NBA. Les altres línies no van mostrar diferències significatives en els efectes genètics directes i materns per a TB, NBA i NW però va haver-hi diferencies significatives per a KI. Es va obtindre una heterosis gran i rellevant per a TB en l'encreuament HxV, seguit pels encreuamentsAxH, AxV i LPxV. També es va trobar una heterosis favorable i significativa per a KI als encreuaments AxV i LPxV, mentres que per als encreuaments AxLP i LPxH l'heterosis va ser significativa i desfavorable. Les conilles creuades, generalment, van mostrar un major nivell reproductiu en comparació amb la línia V. Les diferències entre la mitjana conjunta dels encreuaments comparada amb la línia V varen resultar important, sent 0.45 per a TB, 0.57 per a NBA, 0.75 per a NW i -2.22 dies per a KI. El contrast entre cada dos línies va mostrar un rendiment semblant i no trobàrem diferències significatives entre els efectes genètics directes i materns.

L'últim capítol d'aquesta tesi té com a objectiu estudiar la longevitat funcional, definida com el nombre de dies entre la primera palpació positiva i la mort o eliminació de la conilla per raons alienes a la producció. D'aquesta manera, la longevitat funcional representa l'habilitat de l'animal per a retardar la seua eliminació involuntària. Es van analitzar les dades de 7,211 conilles mitjançant el Survival Kit 6.0, utilitzant un model de Cox d'efectes fixos i riscos proporcionals. El model va incorporar factors dependents del temps, com el grup-granja-any-estació (GFYS), el nombre de nascuts vius (NBA), grup-orde de palpació positiva (GPPO) i estat fisiològic de la femella (PS). Les línies A, H i V van tindre una habilitat semblant per a evitar l'eliminació, sent més sensibles que la línia LP. La línia LP va tindre el menor risc associat, amb diferències importants a edats tardanes i una probabilitat de ser reemplaçada de 0.39, 0.49

i 0.53 vegades la taxa de substitució de les línies A, H, i V. No trobàrem diferències significatives entre els diferents encreuaments i la línia V, excepte amb l'encreuament entre AxH a favor de línia V. Les diferències entre un encreuament i el seu reciproc, generalment, no va ser significativa, excepte entre als creuaments VxH i HxV, favorable a la HxV, i per als encreuaments LPxH i HxLP, a favor de la HxLP. La línia V va tindre el major risc associat a causa dels efectes genètics directes i aquestes diferències van ser significatives respecte a les línies H i LP. D'altra banda, les diferències als efectes genètics materns van ser xicotets i no significatius, excepte en les línies H i V, sent favorables a la línia V. L'estima dels efectes d'heterosis no segueix la mateixa direcció però van mostrar, en alguns casos, la importància dels encreuaments entre línies especialitzades per a produir conilles encreuades per a la producció intensiva de conills de carn. Així, es va observar que en cicles productius primerencs, el risc associat a les línies pures és major que el risc associat als diferents encreuaments, sent aquest període quan encara no s'ha amortitzat el cost de la conilla. Justament el contrari ocorre en cicles productius tardans (5 cicle o més), quan el cost de la femella ja ha sigut amortitzat.

Chapter 1

# Literature review

The importance of meat production shows up nowadays because of the animal protein insufficiency, especially in the less developed countries. A minimum level of animal protein is needed to maintain public health. So, meat production must receive attention and, in particular, rabbit meat production because of some peculiarities of this species that will be detailed later. So, during this review, we will deal with rabbit production in the world, its importance and features. Actually, genetic improvement programs must be followed to achieve high levels of productivity and bring out the genetic materials which will be explicated later with details.

In general, specialized rabbit lines are needed for the genetic improvement, so we will present a short summary about why we have to select maternal and paternal lines, and which are the criterions that should be used for the foundation and selection of these lines. The obtained direct and correlated responses to selection will be commented.

The long-term selection in finite populations generates inbreeding which offers mechanisms favouring the diminution of frequency of unfavourable alleles,-genetic purging-, and the consequent increase of the frequency of the favourable alleles. This aspect will be also considered. The use of crossbred does allows to crosses between lines use the profit of the effects ofheterosis and complementarity between the lines, break the inbreeding accumulated within the lines and distribute the cost of their development into more animals. Thus, some previous crossbreeding experiments will be presented which were carried out in Spain and other countries.

In order to make wider the scope of the genetic improvement of meat rabbits, a review will be done of the genetic determinism of the traits of economic importance that are related to doe productivity, like litter size components, litter size, kindling interval or longevity . The review will present their genetic parameters (heritability, repeatability, genetic correlation with other traits, and the inbreeding and heterosis effects). Concerning to longevity, it is important, also, to clarify its economic importance and to indicate what problems there are for its study.

Finally, a list of some specialized lines, widely distributed at commercial level, will be presented; but we will discuss in detail the Spanish lines, which will be used in this study.

## 1.1 **Rabbit production**

Now most of the rabbit meat production is concentred in countries of the Mediterranean area (Europe and North Africa). In 2010 the world rabbit meat production was 1,668,400 tonnes, with China being the largest producer with 663,000 tonnes, followed by European Union with 472,648 (within this region Italy is the first with 247,500 tonnes, followed by Spain with 70,000 tonnes), (FAO-STAT, 2010).

Rabbit could be considered to be very efficient producing meat. It can turn 20 per cent of the proteins it eats into edible meat. Comparable figures for other species are 22 to 23 per cent for broiler chickens, 16 to 18 per cent for pigs and 8 to 12 per cent for beef, so that with its fast production cycle might be an effective part of the solution for animal protein crisis, especially in the less developed countries (Lebas *et al.,* 1997).

Also, a similar calculation for the energy cost of these proteins is even more unfavourable to ruminants. When cattle or sheep are raised for meat production, most of the energy consumed by the herd or flock is used to maintain breeding females which have a low prolificacy, a maximum of 0.8 to 1.4 young per year against 40-60 for female rabbits because the female has a short period of pregnancy and a great ability to reproduce. So, the female rabbit can produce up to 80 kilograms of meat per year.

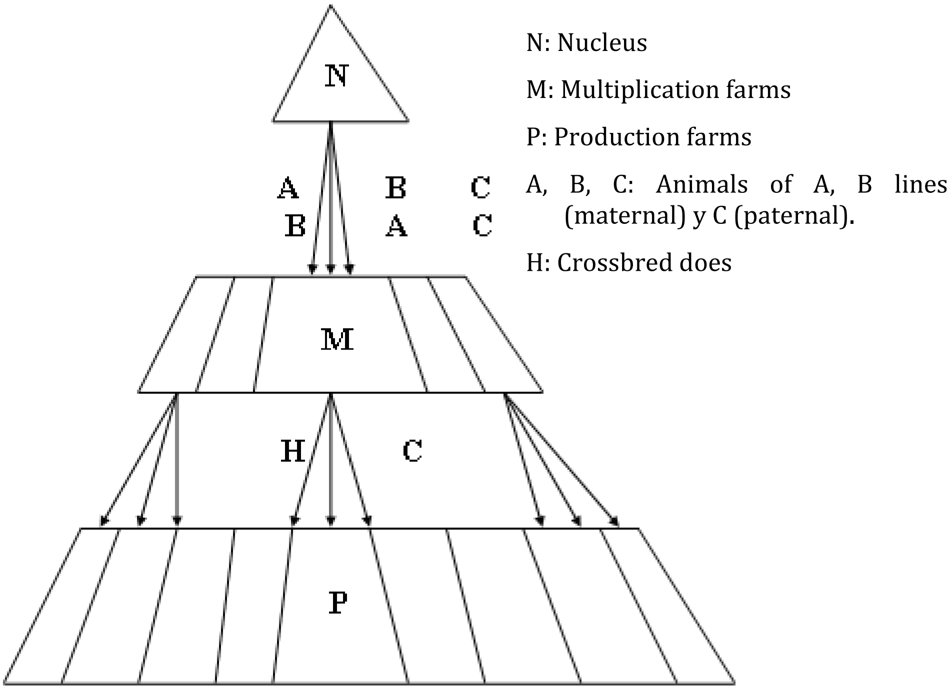
Even with the theoretical lower energy cost per unit of output when cattle are raised for both milk and beef, rabbit meat is still more economical in terms of feed energy than this dual purpose cattle production system. Rabbit meat production is therefore an attractive proposition, especially when the aim is to produce animal protein of good quality. Rabbits can also easily convert the available proteins from cellulose-rich plants, whereas it is not economical to feed these to chickens and turkeys - the only animals with higher energy and protein efficiency. For countries with no cereal surpluses, rabbit meat production is thus highly recommended.

## 1.2 Genetic improvement in rabbits

The objective of a genetic improvement program is the development and diffusion of genetic material to the farmers (Baselga, 2004). The scheme of the diffusion of the genetic improvement in rabbit is of pyramid type, similar to other prolific species like pigs or poultry. The peak of the pyramid is represented by the selection of lines (maternal, paternal or multipurpose) which takes place in the selection nucleus. In this context, maternal lines are commonly selected for prolificacy traits, as litter size at birth or at weaning, following within line selection methods. One nucleus of selection with around 120 females can be enough for the replacement of 80 farms with an average of 400 does per farm (Ramón *et al.,* 1996), taking into account a replacement rate of 120% (Ramón and Rafel, 2002).

The genetic improvement achieved in the selection nucleus is generally distributed down to the commercial population throughout a three way crossbreeding scheme (Matheron and Rouvier, 1977; Rochambeau, 1988; Blasco, 1996; Baselga 2004).

In this crossbreeding scheme, a first cross involves two maternal lines to generate crossbred does, which are used as females for production in commercial farms. Crossbred does are expected to show better reproductive performance than the average of purebred does.



N: Nucleus
M: Multiplication farms
P: Production farms
A, B, C: Animals of A, B lines (maternal) y C (paternal).
H: Crossbred does

**Figure I. 1**Scheme of the diffusion of genetic progress

The cross between the maternal lines allows taking advantage of the expected positive heterosis in reproductive traits, the eventual complementarity among the lines, the reduction in the cost of genetic materials and the dissipation of the inbreeding accumulated within the selected lines (Baselga *et al.,* 2003). The usual methods for improving the maternal lines are based on within-line selection and, generally the selection objective is the prolificacy. It is expected that the initial heterosis expressed in the cross will be maintained along the generations of selection and that the genetic progress obtained selecting the maternal lines will be capitalised on top of the heterosis and expressed in the crossbred does (Baselga *et al.,* 2003).

A second cross consists of mating these crossbred does to males of a paternal line in order to produce the rabbits to be slaughtered for meat. The paternal lines are selected to improve feed conversion rate. This is the most economically important trait in rabbit meat production, but measuring individual feed conversion rate is expensive and is not easily implemented on rabbit farms. Indeed, feed conversion rate shows a negative genetic correlation with average daily gain (Piles *et al.*, 2004), which is easy to record with minimum cost. Therefore, this is generally the selection criteria used in the paternal lines that are also selected within line as the maternal lines.

## 1.3 Selection of maternal lines

In a genetic program of rabbit improvement an important point is the selection of maternal and paternal lines (see section 1.2).So, the starting point is to clearly define the specialization of the desired line. The decision to choose a certain trait as a selection goal will depend on its economic weight, its heritability, its variability, and its relationships with other characters. Reproductive traits are often used to select maternal lines, as it has been mentioned.

The selection methods in maternal lines are more complicated than in paternal lines (Baselga, 2004), because males do not express litter size traits by themselves and because the heritability of reproduction traits is much lower. Thus, it is necessary to consider as many own and relatives' records as possible during the genetic evaluation of both does and bucks; however, the accumulation of records has the consequence of increasing the generation interval and could decrease the intensity of selection because some does and bucks will be dead at the moment of selection. Also, for achieving unbiased predictions of breeding values some environmental and physiological effects are needed to be included into the models of evaluation (Armero *et al.,* 1995).

### *1.3.1 Direct selection*

Litter size at birth or at weaning have been the two main selection criteria considered in genetic improvement programs of maternal lines (Rouvier, 1981; Estany *et al.,* 1989; García-Ximenez *et al.,* 1996; Gómez *et al.,* 1996; Brun *et al.,* 1998 and El-Raffa,2000). There are some advantages in considering litter size at weaning compared to using the number of kits born alive; with the first one an indirect consideration of milk production and maternal ability of the does is also taken into account. Also, litter size at weaning has a positive and high genetic correlation with litter size at marketing. The disadvantage in using litter size at weaning as selection criteria is its lower heritability, compared to number of kits born alive. Litter size at 63 days has economic relevance for the farmer but at this age the mortality of kits is mainly determined by environmental factors and not by genetic effects (Garcia *et al.,* 1982). So, it has been preferred to select for litter size at birth or at weaning.

In some selection programs of maternal lines other criteria have been considered, all of them with the objective of improving either maternal ability, the prolificacy or both. Such a criteria are the number of teats (Rochambeau, 1988), the weight at weaning (Garreau and Rochambeau, 2003), the litter weight at weaning or the total milk production (Khalil *et al.,* 2002; Garreau *et al.,* 2004; Al-Saef *et al.,* 2008 and Youssef *et al.,* 2008).

In France, Garreau *et al.*(2008) used the functional longevity as a criterion of selection in a divergent selection experiment based on genetic merit estimated through survival analysis techniques. It was carried out in the INRA 1077 rabbit line.

Finally, another direct selection procedure for improving the efficiency of selection programs is the so called selection for hyperprolificacy. It has been shown to be a successful way to improve litter size at the foundation of lines (Cifre *et al.,* 1998). Recently longevity of females has been introduced as another foundation objective in maternal lines of rabbits (Sánchez *et al.,* 2004, 2008). These two methods will be described with more details in the last section (section 1.10).

### *1.3.2 Indirect selection*

As it will be indicated in section 1.7, many authors tried to improve litter size by indirect selection for uterine capacity or components of litter size, i.e. prenatal survival and ovulation rate (Ibáñez-Escriche *et al.,* 2004, 2006; Blasco *et al.,* 2005; Mocé *et al.,* 2005; Santacreu *et al.,* 2005; Laborda *et al.,* 2011).

### *1.3.3 Direct response for litter size*

As it can be seen, most of the selection programs and experiments focus on prolificacy. Therefore, in this section a review of the estimated genetic response achieved in those experiments is presented.

In general, the response to direct selection, using litter size as the criterion of selection (see section 1.3.1), has been lower than expected.

In mice, Nielsen (1994) reported a significant response and in pigs, the experiment reported by Lamberson *et al.* (1991) or the ones related to selection on hyperprolificacy (Bichard and David, 1985; Sorensen and Vernensen, 1991; Bidanel *et al.,* 1994 and Noguera *et al.,* 1997) has been demonstrated to be effective. However, the genetic progress of litter size at birth in pigs has been lower than expected (Southwood and Kennedy, 1991; Holl and Robison, 2003).

In rabbits, response to direct selection for litter size has also been lower than expected. The foundation of a maternal line, using hyperprolificacy approach, has been a successful way to improve litter size (Cifre *et al.*, 1998). Significant genetic trends in litter size have been reported when mixed model methodology (Sorensen and Kennedy, 1983) has been used to analyse the long and medium term experiments of selection for litter size, but the result of this methodology is model and genetic parameter dependent.

Some responses in litter size traits were estimated exclusively by mixed-model methods (Estany *et al.,* 1989; Rochambeau *et al.,* 1994 and Gómez *et al.,* 1996) and the estimates ranged from 0.05 to 0.13 rabbits born alive or weaned per litter and generation. With the same method García and Baselga (2002a, b) found that the genetic trend was 0.175 weaned per generation in line A and 0.09 in line V. Analysis of the responses to selection performed by comparing with an unselected control population (Rochambeau *et al.,* 1998 and Tudela *et al.,* 2003) or with a control population obtained from frozen embryos (García and Baselga, 2002a, b), resulted in estimated responses between 0.08 and 0.09 total born rabbits, born alive or weaned per litter and generation.

Baselga (2004) summarized the possible causes of this low response as:

(1) Lower than expected values of additive genetic variance for litter size at weaning.

(2) Heterogeneity among parities that can be high.

(3) Negative correlations between direct and maternal effects.

(4) Lower than presumed selection intensity.

### *1.3.4 Correlated responses in litter size*

Research with mice (Bradford, 1969; Land and Falconer, 1969), swine (Zimmerman and Cunningham, 1975; Cunningham *et al.*, 1979;Lamberson and Day,1986 and Casey *et al.*, 1994) and rabbits (Laborda *et al.*, 2011, 2012) has demonstrated that ovulation rate responded to direct selection, but this selection was not very effective in changing litter size. Ibáñez-Escriche *et al.* (2004, 2006) reported, after 3 and 6 generations of selection for ovulation rate, values of direct response of 0.97and 1.8. The correlated responses for total born were 0.32 and 0.49, respectively, but Laborda *et al.* (2011, 2012a,b) showed, in the same population after 10 generation of selection for ovulation rate, that direct response to selection for ovulation rate was relevant, but there was no correlated response on litter size (−0.15 kits), due to an increase in prenatal mortality.

In other study, after 10 generations of divergent selection for uterine capacity, the correlated response obtained by Santacreu *et al.*, (2005) for total born between high and low lines was 2.35 rabbits, mainly because of a higher correlated response in the low line (1.88 rabbits). But, they reported that, although selection for uterine capacity has been proposed as an indirect way of improving litter size (Bennett and Leymaster, 1989; Argente *et al.,* 1997, 2000 and Blasco *et al.*, 2000, 2005), the observed increase in total born caused by selection for uterine capacity was not greater than the improvement obtained from direct selection and the correlated response in number born alive was less than for total born.

Garreau *et al.* (2010) found no significant differences in prolificacy and fertility, between the high and low line, in their experiment of divergent selection for functional longevity.

## 1.4 Long-term selection and inbreeding

Inbreeding is the result of mating between relatives and implies an increase of homozygosis within the population (Falconer and Mackay, 1996). Darwin conducted some of the earliest experiments on the effect of selfing and outcrossing in over 50 plant taxa, and was one of the first to quantify the costs of inbreeding (Darwin 1868, 1876). More recently, inbreeding depression has become one of the most important areas of research in evolutionary biology and conservation genetics. Most of the early literature regarding inbreeding depression focused on measuring its intensity when populations were inbred, and the relationship between the level of inbreeding and inbreeding depression (Lynch and Walsh 1998).

Inbreeding negatively affects the means of the traits, particularly for those related to fitness i.e. reproduction. It is well known that inbreeding depression cannot occur if there are only additive gene effects (Falconer and MacKay, 1996). Thus, the mean of a trait in a population with an inbreeding coefficient F ($\mu_F$), referred to the mean when the inbreeding is 0 ($\mu_0$) and supposing no epistasis is,

$$\mu_F = \mu_0 - 2F\sum_{i=1}^{n} p_i\, q_i d_i$$

where n is the number of loci affecting the trait; $p_i$, $q_i$ the allelic frequencies of gene i and $d_i$ the dominance effect of this gene. If dominance is present (some $d_i \neq 0$), mean values will decline linearly with the level of inbreeding if the theory of directional dominance is accepted. This theory maintains that the values of $d_i$ tend to be positive. This negative effect, called inbreeding depression, is mediated by an increase in the frequency of homozygotes, which have an average for those traits lower than the heterozygotes. The inbreeding depression can be important in small closed populations (Sewalem *et al.*, 1999; Thompson *et al.*, 2000). Furthermore, an increased rate of inbreeding also means an increase in terms of the variance of genetic gain (Meuwissen, 1991), and a reduction of the additive genetic variance. The selection in finite populations has cumulated effects, increasing inbreeding and reducing genetic gain (Verrier *et al.*, 1990; Wray *et al.*, 1990; Wray and Thompson, 1990). It is known that the effect of the inbreeding on the mean of traits affected by some types of epistasis (that include dominance interactions) is not linear (Crow and Kimura, 1970; Charlesworth and Charlesworth, 1999; Walsh, 2006).

In thier experiments of inbreeding, Darwin had difficulties to explain the phenomenon that some plants after enduring successive generations of inbreeding, recovered fitness and some of them also exhibited higher fitness than the original populations (Darwin, 1876). Since then, researchers have coined the phrase "purging the genetic load" in reference to the fitness rebound that can occur in intensively inbred populations (Crow, 1970).

In general, three different but related mechanisms must be operating at any finite population subjected to natural and or artificial selection; the first is the increase of inbreeding causing inbreeding depression, the second is genetic purging and the third is the apparition of new alleles as consequence of mutations. The last two lead to a smaller impact of a given inbreeding, because new alleles imply extra heterozygosis and genetic purge decreases the frequency of unfavourable alleles and can remove deleterious recessive alleles, reducing the genetic load (Templeton and Read, 1984; Lacy and Ballou, 1998)

The nature and degree of purging depends on the genetic basis of inbreeding depression. If inbreeding depression is due primarily to strongly deleterious alleles, then purging the genetic load is a plausible mechanism by which populations could reduce the cost of inbreeding.

If inbreeding depression results primarily from deleterious or unfavourable alleles, another important consideration is the magnitude of the effect on fitness components when populations are inbred. With severe inbreeding depression, inbred individuals harbouring deleterious or unfavourable alleles may die or not reproduce to the next generation, effectively removing deleterious or unfavourable alleles from the population. Therefore, the magnitude of purging and the resulting rebound in trait values will be sensitive to the degree to which unfavourable alleles are detrimental to fitness (Hedrick, 1994; Wang *et al.*, 1999; Willis, 1999). Alleles of large effect, those that are lethal or semi-lethal when in homozygous form, will be relatively easily purged from the population (Lande and Schemske, 1985; Charlesworth *et al.*, 1990; Hedrick, 1994; Schultz and Willis, 1995; Wang *et al.*, 1999). Alleles that are only partially deleterious or unfavourable will be more difficult to purge as inbred individuals carrying such alleles will have only slightly reduced fitness relative to individuals that are outbred (Hedrick, 1994; Wang *et al.*, 1999). However, it seems most likely that inbreeding depression is due to deleterious alleles of both large and small effect: a mixed model system (Charlesworth and Charlesworth, 1999; Wang *et al.*, 1999). In such a case, successive generations of inbreeding will purge lethal alleles, while the genetic load resulting from mildly deleterious alleles will persist (Hedrick, 1994; Wang *et al.*, 1999).

There are a wide variety of studies that used different experimental and statistical methods to test the incidence of purging. The common methods to detect the purging of the negative effects of inbreeding were presented by Crnokrak and Barrett (2002) and Hinrichs *et al.* (2007).The first authors summarized that the magnitude of purging can be estimated by using: (1) changes in inbreeding depression with successive generations of inbreeding, (2) relative changes in inbred line fitness components compared to the original outbred fitness components, and (3) the ratio of purged population trait values as a function of the ancestral outbred population values (formed by outcrossing inbred lines). As mentioned above, Hinrichs *et al.* (2007) suggested a new method to detect or investigate the differences between the effects of inbreeding in recent generations from that in the more distant past. The method was applied in a long-term selection experiment. In the next paragraphs we will describe briefly these methods.

Also, Crnokrak and Barrett (2002) commented that it is important to distinguish between purging and adaptation to growth conditions and this distinction rests in part on the use/misuse of an appropriate outbred control group for the purpose of comparing fitness components. An appropriate control group would be one for which the inadvertent selective regime experienced by the inbred lines would also apply. This would require knowing what effect acts on the traits of interest for maintaining and choosing individuals to propagate the inbred lines. Since this selection is inadvertent, knowing its effects and being able to replicate them in the outbred lines is impossible.

### *1.4.1 Calculate the old and new inbreeding for population*

Another method, to detect if the population had been purged or not, was presented by Hinrichs *et al.* (2007). This method investigated differences between the effects of inbreeding in recent ($F_{new}$) generations from that in the more distant past ($F_{old}$). The method was applied in a long-term selection experiment on first-litter size in mice. Hinrichs *et al.* (2007) tested the hypothesis of a differential impact of new and old inbreeding in mice and they found that for litter size new inbreeding was estimated to cause greater depression than old inbreeding. They tested the hypothesis of a differential impact of 'new' and 'old' inbreeding. This method will be explicated in the second paper of this thesis with more details.

In animals, it was observed that inbreeding depression was reduced after long time and this reduction was constant, i.e. it depends less on the accumulated inbreeding than on the inbreeding generated more recently. The new inbreeding could take into account the impact of newly arisen mutations, whereas old unfavourable alleles could have diminished their frequency and, sometimes, left the population. For example, in Irish Holstein-Friesians appears that part of the genetic load for milk production has been purged (Parland *et al.*, 2009).

Gulisija and Crow (2007) develop a method to estimate genetic purging of deleterious recessive alleles, using only genealogical information. They apply the method to a population of Jersey cows with pedigrees around six generations and showed that the reduction of the expressed genetic load could have been 12.6 %. They also indicated that to estimate non negligible effects of purging from alleles of small effects more generations are needed.

In Spain there are several maternal lines of rabbits, founded between 1980 and 2004 with a long history of selection for litter size at weaning, that could be, at least a priori, a good material for estimating the difference between the effects of the old and recent inbreeding using the method of Hinrichs *et al.* (2007).

## 1.5 Crossbreeding

Crossbreeding is an alternative to improve performance because of differences between populations. There are two reasons to consider crosses between lines. First, to combine the best features of each line that is called complementarity. The second reason is heterosis (hybrid vigour), wherein, the F1 is commonly superior for some traits to the average of parental lines. Extra benefits can be obtained from heterosis and from the break of the cumulated inbreeding during the selection process. The extent of heterosis will depend on dominance and is proportional to the square of the difference in gene frequency between lines (Falconer and Mackay, 1996).

In crosses between lines often is distinguished between individual and maternal heterosis. Individual heterosis is enhanced performance in a crossbred individual, while maternal heterosis is enhanced maternal performance because the dam is crossbred.

The diallel cross has become a common method of analysing genetic variability among a set of lines and their crosses. A full diallel cross helps to identify superior cross combinations, provides information regarding the relative importance of certain kinds of specific combining abilities and indicates whether extensive crossing is needed to exploit non-additive genetic variation. A diallel analysis that allows the estimation of maternal effects is needed to determine whether reciprocal crosses are likely to be equivalent between them or not.

Numerous experiments, crossing different breeds, lines or strains of laboratory animals have been conducted with rabbits, mice, rats and guinea pigs. In Spain, the studies of crossbreeding were started in the mid-90's and several studies were carried out crossing lines selected or funded on different criteria (Cifre *et al.*, 1998; Gómez *et al.*, 1999, Baselga *et al.*, 2003; Orengo *et al.*, 2003; Piles *et al.*, 2006b), but these studies do not face in a comprehensive way the possibilities of crossbreeding of the current maternal lines. Thus, Cifre *et al.* (1998) studied the possible existence of heterosis in the first generations of H line which was founded from genetically heterogeneous sources. Recently, the crosses between three maternal lines of the Polytechnic University of Valencia (UPV) (lines A, V and H) were evaluated (Baselga *et al.*, 2003). The experiment was designed as a complete diallel cross involving the three lines to analyse the reproductive traits and kindling interval.

There are other studies between the lines of the Department of Animal Science (UPV, Valencia), and the lines of the Rabbit Science Unit (IRTA, Barcelona). Orengo *et al.* (2003) have studied the cross between the lines A, V and Prat (IRTA, Spain) to estimate individual heterosis for litter size traits. A crossbreeding experiment among 5 selected lines (A, V, and Prat as maternal lines and R and C lines as paternal lines providing the terminal sire) was carried out to improve knowledge about the genetic determination of growth traits during the fattening period (Orengo *et al.*, 2009). Piles *et al.* (2006b) published a study about crossbreeding parameter estimation for functional longevity in three maternal lines of rabbits. The lines considered in this study were A, V and Prat. To the best of our knowledge, the previous study is one of the two studies that were carried out to compare the longevity in pure lines and their crosses. The other is the paper by Lukefahr and Hamilton (2000).

Other studies between the Department of Animal Science (UPV, Valencia) and research institutions of other countries were carried out. In Egypt, V line was used in cross with the local lines not only to evaluate the crossbred does but to produce synthetic lines. It was thought that these synthetic lines could be appropriate to produce meat rabbits under industrialized and hot climate conditions in Egypt. All these lines were more fully described by Ragab and Abou Khadiga (2010). Three replicates of V-line were maintained as pure lines and were also used to produce synthetics: one synthetic line, called Alexandria, come from the cross Black Baladi x V and now is selected for post weaning daily gain (El-Raffa, 2000); a second one (Sinai Gabali x V), the Moshtohor line which is selected for litter weight and live weight at 56 days, and a third one is APRI line which was formed from the cross Baladi Red x V. It is selected for litter weight at weaning (Youssef *et al.*, 2008).

In Saudi Arabia, V line rabbits were imported in 2000 and were crossed with one desert Saudi breed (Saudi Gabali) to produce two synthetics, maintaining, also, a replicate of the line V. There were some evidences that V line rabbits and their crosses could produce efficiently under hot climatic conditions (Khalil *et al.*, 2002). The lines are selected for litter weight at weaning and individual weight at 74 d.

In France (the INRA, SAGA, Toulouse), Brun *et al.* (1998) and Brun and Baselga (2005) evaluated some reproductive traits and body weight of does pertaining to the line 2666. This line was formed by crossing the INRA 2066 line and the V line from the UPV.

Khalil *et al.* (1995) performed a crossbreeding experiment in Egypt involving a local breed (Baladi Red) and New Zealand White to estimate direct heterosis, maternal additive effects and direct additive effects on some litter traits and reproductive intervals in rabbits. Other study was carried out to estimate crossbreeding parameters involving Egyptian Gabali and New Zealand White rabbits (Iraqi *et al.*, 2006).In France, the lines named A2066 and A1077 were crossed to obtain the crossbred doe 1067. In 1994, Brun and Saleil (1994) gave estimates of the heterosis for the cross of these lines for total born, born alive and number weaned, the experiment being carried out in farm conditions. Nofal *et al.* (1996), in Hungary, gave values of heterosis for the same traits previously cited for the cross between New Zealand White and Californian. Many works were carried about the crossing between New Zealand White and Californian lines by Lukefahr *et al.* (1983), Lukefahr and Hamilton (2000) and Ouyed and Brun (2008).

### 1.5.1 Analysis of crossbreeding experiments

Several models have been developed to analyze crossbreeding experiment, differing between them in the number and type of parameters considered that rely more or less directly on thedifferent ways of gene action; additivity, dominance and the types of epistasis (Griffing, 1956; Dickerson, 1969; Kinghorn, 1982; Hill, 1982). The experiments of crossbreeding commonly allow the estimation of a reduced number of parameters which oblige to a simplification of the models and the subsequent reparametrization (Wolf *et al*., 1995). One of the most used models is the Dickerson´s model that is based in parameters associated to the populations involved (breeds, lines and interactions between them) in the crosses, referred to their eventual participation in the crossbreds themselves, in the dam or in the sire, etc. Thus, if a model with direct and maternal effects is assumed without recombinational losses, the expected performance $Y_c$ of the crossbred c can be written, following the Dickerson´s model as:

$$Yc = \mu + \sum_{i=1}^{n} \lambda_j g_j^I + \sum_{i=1}^{n} \beta_k g_k^M + \sum_{l \neq m} \gamma_{lm} h_{lm}^I + \sum_{r \neq p} \delta_{rp} h_{rp}^M$$

where, n is the number of lines; $g_j^I$ is the direct genetic effectof the line $i$, being $\lambda_j$ the gene proportion which $j$ contributes to c, so $\sum \lambda_j = 1$; $g_k^M$ is the maternal genetic effect of the line $i$, being $\beta_k$ the gene proportion which$k$ contributes to the dams of c, so $\sum \beta_k = 1$; $h_{lm}^I$ is the direct heterosis between lines $i$ and $j$, being $\gamma_{lm}$ thecontribution of the lines $l$, $m$ to the heterosis of c, so $\sum \gamma_{lm} \leq 1$; $h_{rp}^M$ is the maternal heterosis between the lines $r$ and $p$, being$\delta_{rp}$ the contribution of the lines $r$, $p$ to the heterosis of c dams, so $\sum \delta_{rp} \leq 1$.

According to the previous model, the expected performances of the does of a complete diallel cross of four lines (A, V, H and L), is given in Table I. 1.

From the previous example, the expected performance for $A$line is $Y_{AA} = g_A^I + g_A^M$, while the expected performance of a cross with line $A$ as a sire and $V$ as a dam is $Y_{AV} = \frac{g_A^I+g_V^I}{2} + g_V^M + h_{AV}^I$. Conversely, the expected performance of the reciprocal cross is $Y_{VA} = \frac{g_A^I+g_V^I}{2} + g_A^M + h_{AV}^I$.

The analysis of the data of an experiment of crossbreeding allows the computation of estimable functions of the performances of the different genetic groups involved and the corresponding variance-covariance matrix of their errors. The previous estimable functions can be expressed as linear combinations of some functions of the Dickerson parameters. The latter functions could be estimated using a generalized least square approach (Baselga *et al.*, 2003).

**Table I. 1** Coefficients of expected contribution for genetic effects in different genetic component groups of purebreds and crossbreds

| | λ´s | | | | β´s | | | | γ´s | | | | | |
|---|---|---|---|---|---|---|---|---|---|---|---|---|---|---|
| C | $g_A^I$ | $g_V^I$ | $g_H^I$ | $g_L^I$ | $g_A^M$ | $g_V^M$ | $g_H^M$ | $g_L^M$ | $h_{AH}^I$ | $h_{AV}^I$ | $h_{AL}^I$ | $h_{HL}^I$ | $h_{HV}^I$ | $h_{LV}^I$ |
| AxA | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| AxV | 0.5 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| AxH | 0.5 | 0 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| AxL | 0.5 | 0 | 0 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 1 | 0 | 0 | 0 |
| VxA | 0.5 | 0.5 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 |
| VxV | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| VxH | 0 | 0.5 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| VxL | 0 | 0.5 | 0 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 |
| HxA | 0.5 | 0 | 0.5 | 0 | 1 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 |
| HxV | 0 | 0.5 | 0.5 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 |
| HxH | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 0 |
| HxL | 0 | 0 | 0.5 | 0.5 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 1 |
| LxA | 0.5 | 0 | 0 | 0.5 | 1 | 0 | 0 | 0 | 0 | 0 | 1 | 0 | 0 | 0 |
| LxV | 0 | 0.5 | 0 | 0.5 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 | 0 |
| LxH | 0 | 0 | 0.5 | 0.5 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 | 1 |
| LxL | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 1 | 0 | 0 | 0 | 0 | 0 | 0 |

$g_i^I$: direct genetic effect of line i; $g_i^M$: maternal genetic effect of line i; $h_{ij}^I$: direct heterosis effect between lines i and j; $\lambda_j$: the gene proportion which $j$ contributes to c; $\beta_k$: the gene proportion which $k$ contributes to the dams of c; $\gamma_{lm}$ the contribution of the lines $l$, $m$ to the heterosis of c.

Next, I will present a revision on genetic parameters for litter size traits, the most important traits considered in the aforementioned selection programs of maternal lines, which are the traits to be analysed in this thesis.

## 1.6 Genetic parameters of litter size

Litter size, as it has been said before, has been the objective of selection in several programs involving rabbit populations. The litter size as a character for genetic analysis is complicated by having two components: one attributed to the fertility of the mother of the litter and the other attributed to the paternal viability of the young in the litter (Bowman and Falconer, 1960). The knowledge of variance components and genetic parameters of litter size traits is important to establish the breeding program, to predict how much we can improve these traits and for monitoring the process of selection along the time. The models used for the genetic analysis and evaluation of these traits in animals are, commonly, animal models of repeatability.

### *1.6.1 Heritability and repeatability*

Reviewed estimates of heritability and repeatability for litter size traits are presented in Tables I. 2, I. 3 and I. 4, where it can be seen that the estimates use to be lower than 0.15 for the heritability and lower than 0.25 for the repeatability. The average of the estimates for total born (TB) and number born alive (NBA) are a little higher than for number weaned (NW) or number marketed (NM).

#### *Permanent environmental effects*

Generally, the ratio between the variance of permanent environmental effects and phenotypic variance ($p^2$) is between 10 and 20% (Gómez *et al.,* 1996; Lukefahr and Hamilton, 2000; Rochambeau, 1997; Rastogi *et al.,* 2000; García and Baselga, 2002a, b). Lower estimates of $p^2$ have been reported by Ferraz *et al.* (1992), Baselga *et al.* (2003) and Costa *et al.* (2004). Higher estimates were obtained by Al-Saef *et al.* (2008).

**Table I. 2**Reviewed estimates of heritability ($h^2$) and repeatability (r) estimated by animal models for total born (TB) in rabbits.

| Traits | $h^2$ | r | Breeds/Lines | References |
|---|---|---|---|---|
| TB | 0.07<br>0.03 | 0.19<br>0.17 | A<br>V | Baselga *et al.* (1992) |
| | - | 0.10 | NZW, CAL | Ferraz *et al.* (1992) |
| | 0.08<br>0.08 | - | CAL<br>NZW | Ferraz and Eler (1994) |
| | 0.13 | 0.21 | NZW, CAL | Lukefahr and Hamilton (1997) |
| | 0.08 | 015 | H | Cifre *et al.* (1998) |
| | 0.06 | - | WP | Garreau *et al.* (2000) |
| | 0.10 | - | Caldes | Gómez *et al.* (2000) |
| | 0.09 | 0.30 | NZW | Rastogi *et al.* (2000) |
| | 0.19 | 0.19 | Danish white | Sorensen *et al.* (2001) |
| | 0.10 | 0.22 | V | García and Baselga (2002a) |
| | 0.15 | 0.24 | A | García and Baselga (2002b) |
| | 0.14<br>0.11<br>0.10 | - | A<br>Prat<br>V | Piles *et al.* (2006c) |
| | 0.04 | 0.22 | V, SG | Al-Saef *et al.* (2008) |
| | 0.08 | 0.13 | CPC-Italy | Mantovani *et al.* (2008) |
| | 0.01 | 0.34 | APRI, V | Youssef *et al.* (2008) |

CAL: California; NZW: New Zealand White; WP: White Pannon; SG: Saudi Gabali.

### *1.6.2 Genetic correlation with other traits*

It is important in a selection program to know the genetic correlations between the criterion of selection and other important traits (growth traits, kindling interval, longevity…etc.). The genetic correlation between litter size traits are positive and high, showing the closeness of the genetic determinism of these traits (Sorensen *et al.,* 2001; García and Baselga, 2002a; Nofal *et al.*, 2008).

García and Baselga (2002a) reported that the permanent correlation of total born and number born alive with litter size at weaning and marketing was positive. This correlation between litter size at weaning and at slaughter was equal to 1.00.

Regarding the relationship to growth traits, Khalil *et al.* (1987) and Nofal *et al.* (2008) found high positive genetic correlations between litter size traits and body weight traits. In other study, Camacho and Baselga (1990) estimated the genetic correlations between litter size at weaning and several growth traits in lines A and V, maternal lines selected for litter size at weaning. They obtained estimates of -0.02 and -0.30 for weaning weight, 0.00 and -0.28 and for slaughter weight and 0.04 and -0.23 for growth rate during the fattening period in lines A and V, respectively. García and Baselga (2002b) also estimated the genetic correlations between litter size at weaning and growth traits in the V line. They found estimates which did not significantly differ from zero, being of 0.049, 0.077 and -0025, for weaning weight, slaughter weight and average daily gain respectively. Moreover, they did not find any significant correlated response for these traits.

**Table I. 3**Reviewed estimates of heritability ($h^2$) and repeatability (r) estimated by animal models for number born alive (NBA) in rabbits.

| Traits | $h^2$ | r | Breeds / Lines | References |
|---|---|---|---|---|
| NBA | 0.06 | - | NZW, CAL | Ferraz *et al.* (1992) |
| | 0.07 | 0.19 | A | Baselga *et al.*(1992) |
| | 0.03 | 0.17 | V | |
| | 0.08 | - | NZW | Afifi and Khalil (1992) |
| | 0.11 | | CAL | |
| | 0.27 | - | NZW | Krogmeier *et al.* (1994) |
| | 0.12 | | HL | |
| | 0.07 | - | A1077 | Rochambeau *et al.* (1994) |
| | 0.06 | | A2066 | |
| | 0.09 | - | CAL | Ferraz and Eler (1996) |
| | 0.03 | | NZW | |
| | 0.08 | 0.15 | H | Cifre *et al.* (1998) |
| | 0.07 | - | Caldes | Gómez *et al.* (2000) |
| | 0.12 | 0.32 | NZW | Rastogi*et al.* (2000) |
| | 0.05 | - | Botucatu | Moura *et al.* (2001) |
| | 0.13 | - | A | Baselga and García (2002) |
| | 0.07 | | V | |
| | 0.07 | - | A1077 | Bolet and Saleil (2002a) |
| | 0.06 | - | A2066 | Bolet and Saleil (2002b) |
| | 0.07 | - | A9077 | Bolet and Saleil (2002c) |
| | 0.07 | 0.17 | V | García and Baselga (2002a) |
| | 0.13 | 0.21 | A | García and Baselga (2002b) |
| | 0.12 | - | A | Piles *et al.* (2006c) |
| | 0.08 | - | Prat | |
| | 0.07 | - | V | |
| | 0.015 | - | LP | Sánchez *et al.* (2008) |
| | 0.07 | 0.19 | V | Abou Khadiga (2008) |
| | 0.11 | 0.30 | APRI | |
| | 0.05 | 0.11 | CPC-Italy | Mantovani *et al.* (2008) |

CAL: California; NZW: New Zealand White; HL: HelleGrosilber.

**Table I. 4**Reviewed estimates of heritability ($h^2$) and repeatability (r) estimated by animal models for number weaned (NW) and number marketed (NM) in rabbits.

| Traits | $h^2$ | r | Breeds / Lines | References |
|---|---|---|---|---|
| NW | 0.07<br>0.02 | 0.13<br>0.10 | A<br>V | Baselga *et al.*(1992) |
| | 0.11 | - | NZW | Afifi and Khalil (1992) |
| | 0.10 | - | NZW-CAL | Ferraz and Eler (1994) |
| | 0.23<br>0.05 | - | NZW<br>HL | Krogmeier*et al.*(1994) |
| | 0.08 | 0.13 | A1077 | Rochambeau *et al. (*1994) |
| | 0.09 | 0.12 | NZW | Ayyate *et al.* (1995) |
| | 0.00<br>0.10 | - | NZW<br>CAL | Ferraz and Eler (1996) |
| | 0.04 | - | Prat | Gómez *et al.*(1996) |
| | 0.06 | - | NZW, CAL | Lukefahr and Hamilton (1997) |
| | 0.06 | 0.12 | H | Cifre *et al.* (1998) |
| | 0.04 | - | A2066 | Rochambeau *et al. (*1998) |
| | 0.03 | - | Caldes | Gómez *et al.*(2000) |
| | 0.09 | 0.25 | NZW | Rastogi *et al.*(2000) |
| | 0.03 | - | Botucatu | Moura *et al.* (2001) |
| | 0.08 | - | Danish white | Sorensen *et al.* (2001) |
| | 0.04 | - | A1077 | Bolet and Saleil (2002a) |
| | 0.04 | - | A2066 | Bolet and Saleil (2002b) |
| | 0.04 | - | A9077 | Bolet and Saleil (2002c) |
| | 0.05 | 0.13 | V | García and Baselga (2002a) |
| | 0.11 | 0.17 | A | García and Baselga (2002b) |
| | 0.11<br>0.06<br>0.04 | - | A<br>Prat<br>V | Piles *et al.* (2006c) |
| | 0.08 | - | LP | Sánchez *et al.* (2008) |
| | 0.05 | 0.16 | V, SG | Al-Saef *et al.*(2008) |
| | 0.01 | 0.20 | APRI, V | Youssef *et al.*(2008) |
| NM | 0.07<br>0.01 | 0.12<br>0.08 | A<br>V | Baselga *et al.*(1992) |
| | 0.06 | 0.11 | H | Cifre *et al.* (1998) |
| | 0.05 | 0.12 | V | García and Baselga (2002a) |
| | 0.12 | 0.17 | A | García and Baselga (2002b) |

CAL: California; NZW: New Zealand White; HL: HelleGrosilber; SG: Saudi Gabali

Garreau *et al.* (2000) estimated a low, although positive, genetic correlation between litter size at birth and the weight at week 10 and the daily gain in the fattening period. Their study was performed in a population selected for growth rate and they did not find any significant genetic trend on litter size.

Low estimates of genetic correlation between litter size at birth and litter weight at weaning have been obtained by several authors (-0.06 by Gomez *et al.,* 2000 and 0.13 by Nofal *et al.*, 2008).

Rinaldo and Bolet (1988) showed that after seven generations of selection for litter size at weaning, neither the number of litters per doe nor the length of the productive life was affected. While, Pannu *et al.* (2005) found that the genetic correlation between litter size at birth and kindling interval was negative.

### *1.6.3 Inbreeding depression*

The selection in finite populations has cumulated effects, increasing inbreeding and reducing the genetic gain (Verrier *et al*., 1990; Wray *et al*, 1990; Wray and Thompson, 1990). Consequently, the average of many traits, particularly the ones related with reproduction, is negatively affected. In rabbits, Moura *et al.* (2000) have estimated the magnitude of the depression caused by a 10% of inbreeding of the doe and it resulted to be 0.81 and 0.59 young per litter on litter size at birth and at weaning, respectively. In the same context, Chai (1969), Ferraz *et al.* (1991) and Park *et al.* (1991) also noted a consistent reduction in litter size at birth and at weaning as a consequence of inbreeding.

The inbreeding depression of litter size in mice was demonstrated long time ago by Bowman and Falconer (1960) who found that the decline of litter size was linear with respect to the inbreeding coefficient. The rate of decline was 0.56 young per 10% increase of inbreeding. More recently Hinrichs *et al.* (2007) showed an inbreeding depression of -4.24 pups per unit of inbreeding.

In swine, Bereskin Ben*et al.* (1968) observed that the inbreeding of the sire of the litter had little or no effect on litter size at farrowing. The inbreeding of the dam, significantly, depressed litter size at birth but had no effect on the number of weaned kits. The inbreeding of the litter showed, practically, no influence on litter size at birth but evidenced a significant effect on number weaned.

### 1.6.4 Heterosis effect

Crossbreeding exploits the effects of heterosis and complementarity between lines and it could be successfully employed in rabbit breeding for increasing productivity. Heterosis is the difference in performance between crossbred animals and the average performance of their parents. It is attributed to genes with dominant and epistatic effects. The heterosis can be seen as the counterpart of the inbreeding depression. Traits most affected by heterosis are those pertaining to fitness (litter size, longevity, reproduction rate, etc.). Estimates of direct heterosis for litter size traits, obtained in different crossbreeding experiments, are presented in Table I. 5.

**Table I. 5**Reviewed estimates of direct heterosis (as percentage) estimated for total born (TB), number born alive (NBA) and number weaned (NW).

| Crossed does | TB | NBA | NW | Reference |
|---|---|---|---|---|
| CAL x NZW | 10.5 | | 12.0 | Lukefahr *et al.* (1983) |
| A1077 x A2066 (1067) | 15.2 | 20.1 | 6.7 | Brun and Saleil (1994) |
| NZW x CAL | 12.5 | 10.0 | 5.5 | Nofal *et al.* (1996) |
| NZW x Baladi Red | -2.0 | -3.8 | 6.9 | Khalil *et al.* (1995) |
| V x A2066 | 13.6 | 20.7 | | Brun *et al.* (1998) |
| G x NZW | 18.3 | | 18.8 | Khalil and Afifi (2000) |
| Altex x NZW | | | 0.0 | Medellin and Lukefahr (2001) |
| CAL x NZW | 5.4 | 3.0 | 41.9 | Prayaga and Eady (2002) |
| F x NZW | 12.0 | 11.3 | 25.5 | |
| A x V | 4.8 | 5.5 | | Baselga *et al.* (2003) |
| A x H | 6.9 | 9.8 | | |
| V x H | 1.7 | 1.2 | | |
| A x V | 2.26 | 3.7 | 0.0 | Orengo *et al.* (2003) |
| A x Prat | 13.0 | 16.0 | 16.0 | |
| V x Prat | 10.0 | 8.0 | 7.0 | |
| V x A2066 (2666) | 18.3 | 24.4 | 21.0 | Brun and Baselga (2005) |
| V x Baladi Black | 1.6 | 2.5 | 5.9 | Nofal *et al.* (2005) |
| V x Saudi Gabali | 8.5 | | 2.0 | Khalil *et al.* (2005) |
| G x NZW | -4.03 | | 7.4 | Iraqi *et al.* (2006) |
| Different lines | 2.4 | | 8.95 | Abdel-Azeem *et al.* (2007) |
| V x Saudi Gabali | 5.3 | | 9.1 | Al-Saef *et al.* (2008) |
| V x Baladi Red | 23.9 | | 27.7 | Youssef *et al.* (2008) |

CAL: Californian, NZW: New Zealand White, G: Egyptian Gabali, F: Flemish

The direct heterosis, in most studies, had a positive effect on total born and number born alive and it was always positive for litter size at weaning. Negative values were obtained in few studies for total born and number born alive (Khalil *et al.*, 1995; Iraqi *et al.*, 2006). These heterotic effects may come partly from the genetic distance between the lines or breeds and from the dominance and epitasis gene action modes; but also partly from the inbreeding accumulated in the parental lines, reproductively closed for many generations, which at crossing get disappeared (Brun and Baselga, 2005; Xu, 2003).

## 1.7 Litter size components

After reviewing litter size in the previous section, it is important to study its components in order have a better understanding of the nature of their genetic control. Litter size is limited by the number of ova produced and depends on fertilization rate, and pre- and post-implantation embryonic mortality. So, in this section, we will review the previous genetic studies about litter size components, its importance, summary of how to measure these traits and its genetic parameters.

The knowledge of components of litter size in lines and breeds provides useful pointers for better utilization strategies due to the higher heritability of some of them. There are several selection experiments, indirect methods of selection to increase the litter size, for components of litter size like uterine capacity (maximum number of foetuses a dam can support until birth when the number of ova shed is not a limiting factor), ovulation rate and ovulation rate jointly with litter size. These experiments were carried out in pigs (Cunningham *et al.*, 1979; Neal *et al.*, 1989 and Rosendo *et al.*, 2007), mice (Land and Falconer, 1969 and Bradford, 1969) and rabbits (Argente *et al.*, 1997 and Laborda *et al.*, 2011, 2012).

Ovulation rate is the total number of ova shed by the ovaries at ovulation. In rabbits, ovulation is induced by the coitus stimulus. The procedure to record the components of litter size usually implies observing the reproductive tractus after embryo implantation by laparoscopy or other techniques, and counting the number of corpus luteum to assess the rate of ovulation. The number of implantation sites and the number of living and dead embryos are then counted to determine embryo viability. Litter size at birth is the last record that would be needed to take for obtaining foetal viability.

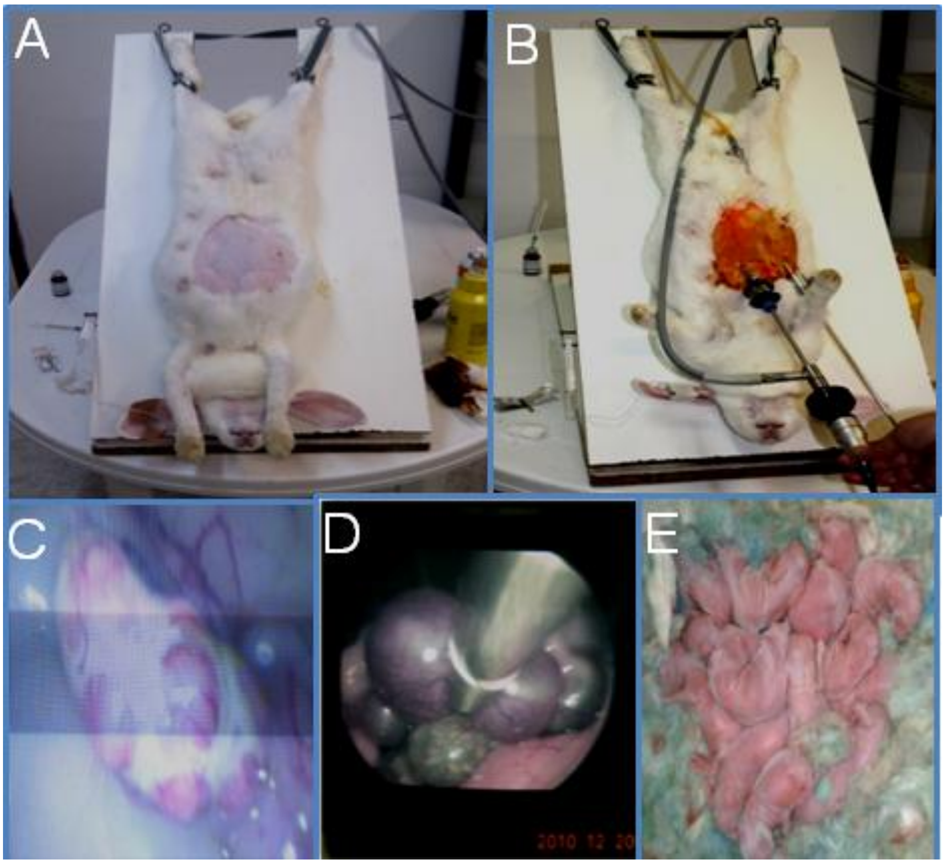


**Figure I. 2**Description of The laparoscopy procedure to record the components of litter size: **A**) prepare and anesthetizing the doe, **B**) ready doe to do laparoscopy and starting to count, **C**) count the number of corpus luteum, **D**) count the number of implanted embryos, **E**) count the number of total born and born alive at parity.

In rabbits, both ovulation rate as well as the other components of litter size is commonly recorded by laparoscopy, after dissection of the reproductive tract. The measurements *in vivo* and *post mortem* of ovulation rate and, also, of implanted embryos, have shown to have a very high correlation coefficient (Santacreu *et al.*, 1990). This indicates that laparoscopy is a very accurate technique to measure ovulation rate and the number of implanted embryos at day 12 of gestation. So, the technique of choice today is the laparoscopy. The effect on the doe is considerably reduced by the use of an endoscope which allows a normal productive life after the operation, and several successive observations on the same female.

Prenatal mortality is around 30% in rabbits (Santacreu *et al.*, 2000; García and Baselga, 2002b; Mocé*et al.*, 2010), about 10-14% corresponding to the embryonic period (pre-implantation), and 20-22% to the foetal period (post-implantation). It is called embryonic period to the period from ovulation to implantation, and foetal period to the period from implantation to birth. There are two mortality peaks in the foetal period, the first between the 8th and the 17th day of gestation and it supposes 66% of the total foetal mortality, the second, between the 18th and 23rd day, and it supposes 27%of the total foetal mortality. In rabbits the prenatal mortality is higher than in mice (20%) and lower than in pigs (40-60%).

### 1.7.1 Heritability

Heritability estimates for ovulation rate varied from low to high values in rabbits. It was estimated to be 0.16 by Laborda *et al.* (2011), 0.44 by Ibáñez-Escriche *et al.* (2006), 0.20 by Argente *et al.* (2000), 0.24 by Bolet *et al.* (1994) and 0.21 by Blasco *et al.* (1993) whereas in swine, it has been found to be 0.17 by Neal *et al*. (1989), 0.33 by Rosendo *et al.* (2007) and 0.42 by Bolet *et al.* (2001) and Ruiz-Flores and Johnson (2001).

The number of implanted embryos had an intermediate heritability (0.32) as in Blasco *et al.* (1993), Bolet *et al.* (1994) and Ibáñez-Escriche *et al.* (2006). Few experiments have estimated the genetic parameters for prenatal survival but, in general, heritability estimates of this trait were low (0.09 by Laborda *et al.*, 2012 and 0.14 by Ibáñez-Escriche *et al.*, 2006) except the one reported by Blasco *et al.* (1993) that was moderate (0.21). In mice, Clutter *et al.* (1990) found that it was 0.15 whereas in pigs, Bidanel *et al.,* (1996), Johnson *et al.,* (1999) and Rosendo *et al.,* (2007) reported estimates between 0.08 and 0.14 Regarding heritabilities of both embryo and foetal survival, in rabbits, Blasco *et al.* (1993) found that it was 0.18 for both traits and in other study, the obtained values for them were 0.26 and 0.35, respectively, (Ibáñez-Escriche *et al.*, 2006).

### 1.7.2 Genetic correlation with other traits

Ibáñez-Escriche *et al.* (2006) reported the genetic correlations between litter size components and, also, between these traits and litter size. They found high values between ovulation rate and litter size (0.57) and number of implanted embryos (0.69), moderate values with foetal survival (-0.46) and prenatal survival (-0.27), and a low value with embryo survival (0.02). The numbers of implanted embryos, embryo survival and prenatal survival had positive genetic correlations with litter size: 0.94, 0.69 and 0.64, respectively. However, a low value was obtained with foetal survival (0.09). Laborda *et al.* (2011) presented the genetic correlations of ovulation rate with litter size (-0.20) and number born alive (-0.29). Other estimates of genetic correlations between ovulation rate and litter size were greater and positive (in rabbits: Blasco *et al.*, 1993 (0.36); in pigs: Johnson *et al.*, 1999 (0.24), and Rosendo *et al.*, 2007(0.41); in mice: Clutter *et al.*, 1990 (0.81), and Long *et al.*, 1991(0.62), although the estimates were very imprecise. In mice, Falconer and Roberts (1960) estimated a positive correlation between ovulation rate and weight at 6 weeks.

### 1.7.3 Inbreeding depression

In rabbits, there are no studies about the inbreeding effect on litter size components. Ovulation rate was not affected by inbreeding, in mice. Thus Falconer and Roberts (1960) did not find differences between inbred and non-inbred females in ovulation rate and foetal mortality, but they found that the inbred females had a high number of embryos lost before implantation which was enough to account for the smaller number of kits born alive per litter.

McCarthy (1967), also in mice, showed evidence of gene dominance affecting ovulation rate and reported that inbreeding had a negative effect on litter size and it was attributable to: 1) a reduction in the ovulation rate of the inbred dams, 2) an increased incidence of embryo mortality which resulted, also, from the dam´s inbreeding. So, it is expected that line crossing will improve ovulation rate and prenatal survival.

### *1.7.4 Heterosis effect*

Few studies have being conducted to assess crossbreeding parameters for litter size components. Bradford and Nott (1969), working with mice, summarized that the observed heterosis on litter size is mainly due to a superior embryo survival of the crossbred, as they shown lower foetal mortality. Also, they confirmed that ovulation rate and embryo survival are controlled by independent genetic systems. They suggest two additional conclusions: 1) pre- and post-implantation survival were, also, controlled by different genes; 2) genes affecting pre-implantation survival exhibit a high degree of dominance, whereas those affecting the other components are more nearly additive.

In rabbits, Hulot and Matheron (1979) and Brun *et al.* (1992) detected positive and significant heterosis for ovulation rate and prenatal survival. In pigs, Bidanel *et al.* (1990) and Galvin *et al.* (1993) did not find heterosis for ovulation rate while, on the other hand, Squiers *et al.* (1952) and King and Young (1957) suggested a considerable degree of dominance for genes affecting ovulation rate. The heterosis of crossbred sows for litter size traits was explained by a high prenatal survival and not by a high ovulation rate (Bidanel *et al.*, 1990; Blasco *et al.*, 1992).

## 1.8 Functional longevity

The longevity in animal production has received attention in livestock species and there is a wide literature dealing with this trait. In this section, some considerations about its economic importance and the difficulties of its study will be given. In addition, it will be reviewed the estimates of its genetic parameters, its variability, among breeds or lines, and its heterosis.

The longevity of reproductive rabbit females has been defined in many different ways: number of litters or length of life (Youssef *et al.,* 2000), number of matings or age at culling or death (Lukefahr and Hamilton, 2000), or culling rate (Tudela *et al.,* 2003), or measured as the number of inseminations that a doe has during its whole life (Garreau *et al.,* 2001). Sánchez *et al.* (2004) defined the functional longevity in rabbits as the time in days between the first positive palpation and death or culling for reasons different to animal production. Each one of these definitions implies different characteristic in the distribution of the records to study; thus, different statistical methods should be used.

### 1.8.1 Economic importance of longevity

In general the main culling reasons in animal production include diseases, low fertility and low production (Vollema, 1998; Sánchez *et al.*, 2004). In animal production the main focus on longevity has been on the productive period from the beginning of reproduction until disposal. Culling for low production is usually referred to as voluntary culling and culling for disease and low fertility as involuntary culling.

Improvement of productive life of does could be interesting because the replacement rate is very high (120%), (Ramón and Rafel, 2002). Rosell (2003) reported that the percentage of does which die or are culled during the first three parities is about 50% or more. The main causes of the end of the productive life of does are death and sickness during the first production cycles, when the cost of the does has not been yet recovered. Due to the high annual replacement rate, the proportion of young does in production is high, and these does are more difficult to handle than the older ones. Consequently, the production is based on immature animals that are significantly less productive. Moreover, the production of animals in the periods of illness before death or culling is significantly limited. All these factors show the importance of enhancing functional longevity in rabbits.

Armero and Blasco (1992) presented a work about the economic weights of several traits in rabbits and commented that a 1% decline in the annual replacement rate is an increase in year profits of 0.34 Euros per doe. In this work, the three most economically important characters were the number of births per year, litter size and average daily gain during the fattening period. The replacement rate stood in eighth place after feed intake in lactation.

So, longevity in rabbits is of economic importance because (1) the higher the number of litters produced by a doe, the greater the opportunity to spread doe costs over a longer period of time;(2) increased longevity tends to extend the parity distribution at the expense of lower parity orders, increasing the number of kits per doe per year through an increased litter size and a reduced replacement rate; and (3) the high replacement rate, when the new animals are bought outside, implies a higher risk of health problems.

### *1.8.2 Difficulties of longevity study*

Longevity records can be considered as difficult to dealt with basically due to two types of reasons: 1) The definition of the trait implies that records are taken late in the animal's life in fact when it is dead- which enlarge the generation interval. This implies that selection candidates must be evaluated essentially by information from relatives. However, as it will be shown later, the heritability of this trait seems to be low. 2) The need of special statistical methods of analysis which allow taking into account the peculiarities of these records. First, survival times are usually a mixture of discrete and continuous data that lend themselves to a different type of analysis than those in the traditional discrete or continuous case. The mixture is the result of censoring that has an important effect on data analysis. Censoring is present when we have some information about a subject's event time, but we don't know the exact event time (right censoring). Thus, for the censored data, if these data are not included in the analysis, or included as complete data, to estimate the average population survival, biased estimates will be obtained. So, a correct consideration of the censored and uncensored data is needed to have unbiased estimates for longevity.

Second, to analyse longevity data is needed to use time dependent factors in the model. On the other hand, the dependent variable (the time to the event of interest) is very asymmetric and generally has an unknown distribution, and consequently the standard methods of analyses relying on the normal distribution are not adequate. The more suitable approach to study longevity is survival methodology, which is based on analysing the hazard, which could have a known parametric distribution or which could be fitted by semi-parametric or nonparametric models. This method also allows the use of factors that change with time and the censored data are included naturally in the analysis. Usually, as the population under study is changing, we only consider the individual risk to die for those who are still alive, but this means that many standard statistical approaches cannot be applied.

### *1.8.3 Variability and heritability within lines*

Recently, longevity has been considered as a selection objective of maternal lines and few estimates of its heritability have been reported (Sánchez *et al.,* 2004, Garreau *et al.,* 2001). Many authors tried to estimate the heritability of longevity from the information coming from the selection programs for litter size. The magnitudes of heritability estimates vary between populations and also depend on the trait's definition and method of analysis, but in general, they are low to moderate. Using linear models and REML methodology, Youssef *et al.* (2000) estimated heritabilities of 0.08 and 0.13 for number of litters and length of productive life, respectively, in rabbits. In another work, Sánchez *et al.* (2004) using a sire-maternal grand sire model and the estimated mode of the sire variance computed a heritability of 0.053, that expressed as effective heritability (Yazdi *et al*., 2002) corresponds to a value of 0.086. Low values of heritability of longevity (0.05, 0.10 or 0.24), depending on the model, were also obtained by Garreau *et al.* (2001)

Piles *et al.* (2006b) analysed functional longevity of 2 selected lines of rabbits (Prat line, selected in Spain, and the A1077 French line). The estimated heritabilities from this work were around 0.16 for both lines, with a model including a physiological status × cycle combined effect, and 0.24 and 0.19 in the Prat and A1077 lines, respectively, with the model without the previous effect. This is an indication in the Prat line of a putative significant genetic correlation between longevity and fertility as the physiological status depends on the female ability to get pregnant back after parturition. Yazdi *et al.* (2000) reported estimates of heritabilities of longevity in Swedish Landrace sows ranging from 0.05 to 0.27, depending on the model used. Gou *et al.* (2001)

reported a heritability of 0.25 for length of productive life in Landrace sows. Serenius and Stadler (2004) reported estimates of heritability of longevity of 0.16 and 0.17 for Landrace and 0.17 and 0.19 for Large White populations using a survival analysis, but lower estimates of 0.05 and 0.10, respectively, using a linear model.

### *1.8.4 Relationship with other traits*

Estimates of the correlation between longevity (log of hazard) and litter size traits in rabbits were found in only one study (Sánchez *et al.,* 2008). They reported an estimated genetic correlation of −0.17, not significantly different from zero. Regarding the environmental correlations, it only could be considered as significantly different from zero (-0.11±0.016) between number born alive and longevity.

In Landrace and Large White, Serenius and Stalder (2004) reported that length of productive life and lifetime prolificacy (number of piglets born alive during sow's length of productive life) had a genetic correlation higher than 0.95. Thus, genetic gain in length of productive life through selection will result in direct genetic gain in lifetime prolificacy and vice versa. The genetic correlation with the number of weaned piglets was 0.30 and 0.39. Also, a moderate negative genetic correlation (−0.40 and −0.43) was found between farrowing interval and length of productive life. Furthermore, they reported both zero and unfavourable genetic correlation between the length of productive life and average daily gain.

### *1.8.5 Heterosis*

Few studies were carried out to estimate the heterosis effect on longevity in rabbits. In a crossbreeding experiment between Californian (CAL) and New Zealand White (NZW) rabbits, Lukefahr *et al.* (1983) found that longevity had an unfavourable heterosis (10%) for the cross between the two breeds. In other work, concerning the same breeds, Lukefahr and Hamilton (2000) reported the superiority of the NZW and crossbred does with respect to the CAL does. Piles *et al.* (2006b) indicated that the estimated value for the individual heterosis for longevity depended on the lines involved in the cross. Thus, for the cross between lines A and Prat, the estimated favourable heterosis effect was −0.349, which was significantly different from zero. For the cross between lines V and Prat, the estimated heterosis was −0.244, while it was not significant for the V × A cross.

In other species, differences in survival also have been observed between breeds, lines, and crossbred animals (in pigs: Hall *et al.*, 2002; Rodríguez-Zas *et al.*, 2003; in goats: Pérez-Razo *et al.*, 2004; in beef cattle: Núñez-Dominguez *et al.*, 1991; Arthur *et al.*, 1993).

### *1.8.6 Variability between breeds or lines and heterosis*

A divergent selection experiment for functional longevity, based on genetic merit estimated through survival analysis techniques, was carried out in the INRA 1077 rabbit line (Garreau *et al.,* 2008). The difference of longevity between the two lines was 0.92 artificial inseminations i.e. 39 days. Also, the proportion of mortality and culling were higher in the low line than in the high line in two farms.

To our knowledge, very few works have been carried out to study genetic variability of rabbit longevity among breeds, lines and crossbred does. In a study by Piles *et al.* (2006a), a complete diallel cross involving three maternal lines of rabbits (A, V, Prat), was performed to estimate cross-breeding parameters for functional longevity. A Cox model (Cox, 1972) that incorporated time-dependent and time-independent factors was used. In this study no maternal genetic effects were detected as significant and its magnitude was generally low. Significant and relevant differences between direct genetic effects were only found for line Prat with respect to line A. Heterosis was found to be significant and favourable between lines A and Prat, and between the lines V and Prat.

Lukefahr and Hamilton (2000) compared Californian (CAL), New Zealand White (NZW) and CAL x NZW does for longevity and accumulated production. Data were analysed, using linear models by ANOVA procedures (Harvey, 1990). The analysis was based on the normal distribution and did not take into account the time-dependent factors and censored data. The NZW had high longevity than the CAL and the crossbred does behaved similarly to New Zealanders. Coudert and Brun (1988) carried out a complete diallel cross between NZW and CAL, and they analyse mortality rate, elimination rate and causes of elimination or death. They did not get differences between direct genetic effects and maternal genetic effects for mortality and elimination rates. The heterosis was significant for both traits, favourable for mortality rate and unfavourable for elimination rate.

Sánchez *et al.* (2008) showed that, in a study to compare the LP line and V line, the probability that a V female left the herd was between 2.40 and 1.72 times higher than that of a LP doe, depending on the farm.

## 1.9 **Genetic parameters of kindling interval**

### ***1.9.1 Genetic variability***

This trait is defined as the number of days between two consecutives parities. Kindling interval is economically important and is a direct indicator of the fertility of the does for a given mating management.

Significant differences in direct genetic effects between lines were found for kindling interval by Baselga *et al.*, (2003). These authors also found that the heritability and ratio of variance of permanent environmental effects to phenotypic variance for this trait were 0.078 and 0.008, respectively. Khalil and Soliman (1989) and Moura *et al.* (2001) estimated the heritability of the interval between parities and obtained values that were close to zero.

Regarding the kindling interval, few studies were carried out in rabbits. Favourable and low heterosis were found (-5.4%) in the cross NZW x Baladi Red (Khalil *et al.*, 1995) and in the crosses AxV (-1.5%), AxPrat (-4%) and VxPrat (-0.47%) (Orengo *et al.,* 2003). In a diallelic cros experiment between A, H and V line, Baselga *et al.* (2003) observed direct heterosis for AxV (-2.73%), AxH (4.15%) and VxH (2.84%). Prayaga and Eady (2002) presented unfavorable heterosis for kindling interval, being 5.3 %, for CALxNZW does and 3.4 %, for the cross between Flemish and New Zealand White.

## 1.10 Commercial maternal lines

Many programs have been carried out to create new lines following the previous selection criteria (see section 1.3.1 and 1.3.2). The beginning of those breeding programs was in France followed by Spain, and then in many countries all over the world. We will pay more attention to the French and Spanish programs because the two programs have a long time selection history and both are still running. We mention the involvement of the INRA in France, and the Department of Animal Science of the UPV and the Rabbit Science Unit (IRTA, Barcelona) in Spain, developing lines to be used in crosses. In France, since the seventies of the twenty century, the INRA (SAGA, Toulouse) has been selecting two maternal lines for litter size traits (INRA1077 and INRA2066). Later, two lines more have been developed. The lines were INRA2666 (from an initial cross between line V and line INRA2066) and INRA1777. Concerning maternal lines in Spain, there are four maternal lines (A, V, H and LP) in UPV and one in IRTA (Prat) (Baselga, 2004).

A brief list of the lines, which are used in commercial farms to produce crossbred does, is presented in Table I.5.

We will give more details of the Spanish program, specially the program of Universidad Politécnica de Valencia (UPV) for development of new specialized lines, because of the large number of maternal lines developed, the different approaches used for their foundation and because these lines will be used in this work. The UPV program was started in 1976 and now there are four maternal and one paternal line, which are under selection.

Line A was initiated in 1976 sampling NZW rabbits, reared by farmers near Valencia (Spain). After three generations without selection, the line has been selected by a family index, since 1980 (Estany *et al.,* 1989) to increase litter size at weaning. The line is kept closed since its foundation and currently it has reached the 41st generation.

**Table I. 6**Some commercial maternal lines selected in different countries.

| Line | Origin[1] | Criteria[2] | Reference | Country |
|---|---|---|---|---|
| INRA1077 | NZW, B | LSW | Rouvier, 1981 | France |
| INRA2066 | CAL, GH | LSB | Brun, 1993 | France |
| INRA2666 | INRA2066, V | LSW | Brun *et al.,* 1998 | France |
| A | NZW | LSW | Estany *et al.,* 1989 | Spain |
| V | 4 specialized lines maternal lines | LSW | Estany *et al.,* 1989 | Spain |
| H | Commercial farms | (Hyperprolificacy), LSW | Cifre *et al.,* 1998 | Spain |
| LP | Commercial farms | (Hyperlongevity), LSW | Sánchez, 2005 | Spain |
| Prat | crossbreds | LSW | Gómez *et al.,* 1996 | Spain |
| APRI | BR, V | LWW | Youssef *et al.,* 2008 | Egypt |
| Moshtohor | Sinai Gabali, V | LWW | Youssef *et al.,* 2008 | Egypt |
| Saudi-1 | Saudi Gabali, V | LWW, BW84 | Youssef *et al.,* 2008 | Saudi Arabia |
| Saudi-3 | Saudi Gabali, V | LWW, BW84 | Khalil *et al.,* 2002 | Saudi Arabia |
| Uruguay-V | V | LSW | Capra *et al.,* 2000 | Uruguay |

[1]. The breed or the line of origin. NZW: New Zealand White; BR: Baladi Red; [2]. The criteria of selection (foundation) of the line. LSW: litter size at weaning; LSB: litter size at birth; LWW: litter weight at weaning.

Line V was founded in 1981 as a synthetic line of four specialised maternal lines. After three generations without selection, the line has been selected (Estany *et al.,* 1989) to increase litter size at weaning. The method of evaluating the animals is a BLUP under an animal-repeatability model. Like line A, this line is kept closed since its foundation and it is currently in its 37th generation.

Line H was founded applying hyperprolific selection and embryo cryopreservation techniques (García-Ximénez *et al.,* 1996). The hyperprolific does were assembled from a large commercial population, spread over different Spanish farms. The hyperprolific does were required to satisfy one or both of the following criteria: to have 20 or more kits born alive in one litter or to have a cumulative number of kits born alive in all recorded parities equal or higher than the threshold corresponding to the best 1% of the set of does with the same number of recorded parities. It was assumed that the does pertained to a population with a mean of 9 rabbits born alive per litter, a standard deviation of 2.65 rabbits per litter and a repeatability of 0.2. A first step was carried out in 1,993 to obtain male progeny (VH males) by hysterectomy from 20 hyperprolific does mated to nine bucks of the different nuclei of line V, line showing a high prolificacy (Baselga *et al.,* 1992). In a second step, a new and larger set of hyperprolific does (87 does) was mated to 47 VH males to obtain progeny (464 animals of 63 days) which constituted generation 0 of line H. After its foundation, the selection criterion has been litter size at weaning.Now, this line has reached the 17th generation.

The line LP was founded selecting does at commercial farms excelling because of their high longevity but being above the mean in prolificacy (Sánchez, 2005 and Sánchez *et al.,* 2008). It was intended to apply a very high intensity of selection for longevity, in a similar way as it was done in rabbits (Cifre *et al.,* 1998) or pigs (Bichard and David, 1985; Sorensen and Vernersen, 1991; Herment and Runavot*,* 1994; Noguera *et al.,* 1997) for prolificacy.

The foundation of the LP line took place in three steps and started in April 2002. The first step tried to get sons from 15 high longevity does, found in 8 commercial farms. The does were inseminated with semen from bucks of the current generation (27) of the V line.

The second step tried to get sons of a new batch of 15 high longevity does, mated to the males got from the first step. The third step was the constitution of the line LP with the progeny of 32 new high longevity does, detected in 25 farms of Spain and Portugal, mated to 17 bucks obtained in the previous step. Like line H, after the foundation LP line is being selected for litter size at weaning (Sánchez *et al.*, 2008) and currently is has reached the 7th generation of selection.

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Chapter 2

# Objectives

The objective of this thesis was to evaluate four maternal lines of rabbits and their crosses and estimate the crossbreeding parameters in a diallel cross experiment. This general objective was translated into the following specific objectives:

1. To compare four maternal lines of rabbits in terms of reproduction traits, at their foundation and at fixed times, using historical data of their selection programs.
2. Using the same data set , to study several items related to inbreeding: i) estimate the effective population size of the lines, as a measure of the rate of increase of inbreeding and ii) study if the inbreeding effect on litter size traits depends on the pattern of its accumulation over time.
3. To compare the genetic groups of a diallel cross between the four maternal lines and estimate the crossbreeding parameters for the following traits:

- Litter size traits (total born, number born alive, number weaned).
- Kindling interval, used as a direct indicator of the fertility of the does.
- Litter size components (ovulation rate, implanted embryos, embryo survival, fetal survival, prenatal survival).
- Functional longevity.

Chapter 3

# A Comparison of reproductive traits of four maternal lines of rabbits selected for litter size at weaning and founded on different criteria

## 3.1 Abstract

The objective of this study was to compare four Spanish maternal lines of rabbits (A, V, H and LP) founded on different criteria but selected for litter size at weaning, since their foundation until present for 41, 37, 20 and 7 generations, respectively. The comparisons among the lines were performed for litter size traits and kindling interval. The first comparison made was at the foundation time of the lines, using mixed animal models (additive and non-additive permanent effects) and using the complete data set (from June 1980 to February 2009) and the full pedigree to take into account the process of selection. A second comparison was made at fixed times and location (during the six year-seasons shared at the same farm and similar conditions for lines A, V and H involving data from March 1997 to August 1998, and A, V and LP lines from September 2007 to February 2009. The models used in the second comparison did not include the complete data set nor the additive genetic effects; therefore, that line comparisons were not dependent on the genetic model.

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This paper has been published in the journal "Livestock Science" with the following reference: Ragab, M., M. Baselga. 2011. A comparison of reproductive traits of four maternal lines of rabbits selected for litter size at weaning and founded on different criteria, *Livest. Sci., 136:201–206.*

The raw means for total born, number of kits bon alive, number of weaned kits and number of marketed kits per litter obtained from 47,132 parities produced by 12,639 does were 9.80, 9.07, 7.79 and 6.95 rabbits respectively, demonstrating the high level of prolificacy of the lines. The kindling interval raw mean was 49.80 days.

At their respective times of foundation, line A showed the lowest litter size with mean differences of this line over the mean of the other lines of 1.39, 1.20, 0.84 and 1.06 for number of total born, born alive, weaned and marketed kits per litter, respectively. Lines V and H did not show significant differences for litter size traits, but for kindling interval the contrast was 3.30±0.72d, which was significant and favourable to line H. LP exceeded V by approximately one rabbit for all litter size traits. The differences between the lines for kindling interval were negligible. Some interactions between lines and farm-year-seasons were important.

In the comparison of lines A, V and H, performed with data corresponding to the period comprised from March 1997 to August 1998, the pattern of the differences between the line A and the others was similar to the one observed at the origin, and the only significant difference was found between lines V and H for the kindling interval (4.62 d in favour of line V). The comparison between the lines A, V and LP,performed with data of the period comprised from September 2007 to February 2009, showed an approximation in their reproductive performance compared to the differences found at the origin. Overall, good agreement was observed between the comparisons of lines for litter size traits at fixed times, using a model without genetic effects and data recorded during the time of comparisons, and the predictions derived from the model with genetic effects. Another point is the importance of the criteria in the sample of founders of lines that were used to determine the initial or starting performance levels. Therefore, it is recommended that commercial rabbit producers utilize line populations selected for the traits of economic interest rather than on a popular breed.

**Key words:** Rabbits, maternal lines, selection, genetic parameters, litter size, kindling interval.

## 3.2 Introduction

The organization of genetic improvement programmes for rabbits is a pyramid type with the peak of the pyramid representing the selection of specialized lines (maternal and paternal lines) in nucleus populations.Developing maternal lines is a crucial activity for companies and public institutions that are devoted to the genetic improvement of meat rabbit production. These lines need to be established on the basis of direct or indirect selection for litter size at birth or at weaning (Estany *et al*., 1989; Garreau *et al*., 2004).

In this context, an important issue is the performance of the lines at their foundation (Baselga, 2004), which defines the starting point from which responses to selection will accumulate. Also, when several nucleus lines share the same farm environment for long periods of time it is possible, using animal models and the complete data set, to define estimable contrasts for comparing the performance of the lines at foundation, regardless of the time of foundation for each line. It is also feasible, without relying on animal models and using only the data recorded in a short period of time, to compare the performance of all lines. In addition, the same comparison made at defined periods of time canbe done to compute genetic trends derived from animal models involving the complete data set. Thus, the agreement of both comparisons could be considered as evidence in favour of the appropriateness of animal models used for data analysis. To our knowledge, this type of analysis has not been done in rabbits, probably because it is not common that several lines share the same nucleus farm in which selection is carried out for many generations. This is the case of four Spanish maternal lines, founded between 1980 and 2004 with a history of selection for litter size at weaning since their foundation. Thus, the main objective of this study is to compare four maternal lines of rabbits in terms of reproduction traits, at their foundation and at fixed times, taking into account the concept that these lines were founded on different criteria but that all lines were selected for litter size at weaning.

## 3.3 Material and methods

### *3.3.1 Animals*

The present study was conducted involving four Spanish maternal lines of rabbits, A, V, H and LP. These lines, after their foundation, have been selected to increase litter size at weaning. The analysis included all the data recorded from the 1st generation to the current 38th, 34th, 15th and 4th generations for lines A, V, H, and LP, respectively.

The animals of A, V and LP lines were maintained as closed nucleus populations since the beginning of the selection process until present and were housed on the same farm of the Animal Science Department, Universidad Politécnica de Valencia. The H line was housed at the same farm until its 10th generation of selection (May 2004) when it was moved to another farm 180 km north of Valencia (San Carlos de la Rápita, Tarragona).

Line A originated in 1980 from New Zealand White (NZW) rabbits reared by farmers near Valencia, Spain. The NZW breed has been commonly accepted as one of the main breeds of rabbits used for meat production. The criteria used to form line A were that the founders were healthy and they fulfilled the standards of the NZW breed. Since 1980, the line has been selected by use of a family index (Estany *et al.,* 1989). Line V was established from four specialised maternal lines in 1984 into a composite synthetic line. The method of evaluating the animals (Estany *et al.,* 1989) is by BLUP under a repeatability animal model, as for lines H and LP. Line H was founded by applying hyperprolific selection and embryo cryopreservation techniques (Cifre *et al*., 1998). The hyperprolific does, used in founding this line, were assembled from several large commercial populations. The LP line is a maternal line and it was founded by selecting females from commercial farms that showed an extremely long productive life (measured as a function of the number of parities) associated with prolificacy (measured as the mean number born alive per parity) near or above the average of the Spanish commercial rabbit population (Sánchez *et al.,* 2008)

Selection was in non-overlapping generations for all lines and does for the next generation were selected from the best evaluated matings. The bucks were selected within sire from the best mating of the sire to contribute a son to the next generation.

Does were first mated around 17 weeks of age. The does were serviced 10-12 days post-kindling and a pregnancytest was carried out by abdominal palpation on day 12 after mating. There was an exception to this mating management for lines V and LP from December 2003 to November 2005 when does were mated 25 days after kindling.The does that did notaccept the buck were presented to the male one week later and does that were not pregnant were also returned then for a repeat mating. Matings between close relatives were avoided by ensuring that mates did not have common grandparents. The equipment used in the nucleus farm was the same for all lines, except that the feeders used from September 1998 to November 2003 were different for the H line.

Litters were reared by their dams, without fostering, for about 28 days. At weaning, rabbits were individually identified by a number tattooed on the ear and placed in collective cages of about nine rabbits until marketing at 63 days. Animals were housed at the experimental farm of the Universidad Politécnica de Valencia in individual cages. They were kept under controlled 16-h light: 8-h dark photoperiods. Rabbits were fed a standard commercial pelleted diet, offered *ad libitum*.

### 3.3.2 Traits

The prolificacy traits studied were: total born**(TB),**number born alive **(NBA),** litter size at weaning **(NW,** 28 d**),** litter size at marketing **(NM,** 63 d**)** and a fertility trait defined by the kindling interval (number of days between two consecutives parities).

### 3.3.3 Statistical analysis

Data were analysed usingtwo-trait repeatability animal models to estimate the variance-covariance components and to compare the lines at their foundation. As selection was applied for litter size at weaning, this trait was included in the analysis for other traits in order to obtain unbiased estimates due to selectionThe model used for litter size traits was as follows:

$$Y_{tijkmnl} = FYS_{ti} + PS_{tj} + L_{tk} + FYSL_{tik} + F_{tm} + a_{tkn} + p_{tkn} + e_{tijkmnl} \quad \text{(Model 1)}$$

Where $Y_{tijkmnl}$ is the $l$ record of the $t$ trait of litter size of the $n$ doe nested to $k$ line, obtained at physiological state $j$, year season $i$ and $m$ inbreeding class; $FYS_{ti}$ is the fixed effect of farm-year-season of the parity (one year season every three months: 132 levels for all traits and 115 levels for NM); $PS_{tj}$ is the fixed effect of the physiological state of the doe (5 levels depending on the parity order and present lactation state of positive insemination where 1 for nulliparous does, 2 (4) for primiparous lactating (non-lactating), and 3 (5) for multiparous lactating (non-lactating)); $L_{tk}$ is the fixed line effect (4 levels); $FYSL_{tik}$is the fixed effect of interaction between farm-year-season and line (291 levels for TB, NBA and NW, and 265 levels for NM), that was included in the models to limit the comparisons between any two lines to the farm-year seasons shared at the same conditions by both lines; $F_{tm}$ is the fixed effect of inbreeding effect (7 levels depending on the inbreeding of the doe, where 1 from 0 to 0.05, 2 from 0.05 to 0.10, 3 from 0.10 to 0.15, 4 from 0.15 to 0.20, 5 from 0.20 to 0.25, 6 from 0.25 to 0.30, 7 from 0.30 to 0.35; $a_{tnk}$is the random effect of the additive value of the doe n, nested in line $k$ and related through the numerator relationship matrix, $\boldsymbol{A}$ (14609 animals); $p_{tnk}$ is the random effect of permanent environmental plus non-additive genetic effects of the doe n (uncorrelated between them and with the other random effects within the same trait but correlated for different traits within individual); $e_{tijkmn}$ is the random residual effect of the model (uncorrelated between them and with the other random effects effects within the same trait but correlated for different traits within individual).

Inbreeding was used as a fixed effect after classifying it into categories, as previously explained, in order to reduce the problem of its co-linearity with farm-year-seasons.

The comparison among lines for kindling interval was carried out by a two-trait repeatability animal model with litter size at weaning being the second trait. The model used for kindling interval was as follows:

$Y_{ijkmnl} = FYS_i + PO_j + L_k + FYSL_{ik} + F_m + a_{kn} + p_{kn} + e_{ijkmnl}$(Model 2)

where$Y_{ijkmnl}$ is the record $l$of kindling interval measured in $i$ farm-year-season (131 levels) and $j$ parity ($PO_j$; 14 levels) of the doe $n$ belonging to$k$ line (4 levels), and having an inbreeding coefficient in class $m$; other components of the model were defined above in Model 1.

The first step of the analysis was to obtain REML estimates of the variance-covariance components of the mixed models used from the data for all generations and lines. A total of 47,132 parities from 12,639 does were included (15,878, 19,280, 8,570 and 3,404 parities for A, V, H and LP, respectively). The pedigree file included 14,609 animals and version 6.0 of the VCE software was used for this analysis (Groeneveld *et al.,* 2008). The second step was to solve the mixed model equations using REML variance-covariance components as estimated in the first step to compute the contrasts used to compare lines at their foundation (different times for each line) and at fixed locations and generation times. The PEST package was used to solve these equations (Groeneveld, 1990).

### 3.3.4 Comparison of lines at their foundation.

This comparison was performed after solving the mixed models given above on the whole data set and computing the corresponding contrasts. The contrast between any two lines for a given trait was an estimable function involving the estimates of the line effects and the estimates of the interactions (farm-year-season x line), corresponding to the farm-year-seasons shared by the two lines under the same environmental conditions. Because the effect of selection is considered in the models by the additive effects, the line effect was represented at the time of foundation of the lines. A value was computed for each line and trait as the sum of the line effect and the average of the interactions of farm-year-season x line corresponding to the line and farm-year-seasons considered. The contrast was the difference between the values computed for each line. Common farm-year-seasons between lines at the UPV farm were from June 1982 to February 2009 for A and V lines, excepting the period between December 2003 and November 2005; from June 1996 to June 2004, for lines A and H, excepting the period between September 1998 and November 2003 and from December 2005 to February 2009 for the lines A and LP. The common farm-year-seasons for lines V and H were between June 1996 and August 1998; and from December 2003 to February 2009 for the lines V and LP. Significance levels were detected as first class error at α=0.05.

### *3.3.5 Comparison of lines at fixed times and locations (observed and expected differences)*

The times chosen for the comparison of lines were the last six farm-year-seasons shared at the same farm and conditions by three lines: from March 1997 to August 1998 for lines A, V and H, and from September 2007 to February 2009 for lines A, V and LP. For these comparisons, the additive genetic effects were excluded from the models and only the data recorded during the shared times of comparison were used. This way, the line effects refer to the real genetic merit of the lines at the time of comparison as a consequence of selection and genetic drift, but not being dependent on the genetic model.Thus, the statistical models used in these analyses were the same as described in the previous section, but the additive genetic effects were not considered.

Concerning variance components used for solving the models, the permanent variance was the sum of the additive genetic variance and the permanent variance of the previous analysis. The residual variance was the same in both analyses. The estimable functions used to obtain contrasts (referred to as observed differences), were computed as explained in the previous section, but here all the farm-year-seasons were shared by the three lines. The first class error was set at α=0.05. Using results of the analysis obtained using models 1 and 2 and involving the whole data set (section 2.3.2), the expected differences between the lines at fixed times can be computed as the contrast between lines during the six farm-year-seasons shared, plus the difference between the averages of the additive genetic values of the animals of each line having litters in the period, weighted by the number of litters. These expected estimates depend on the genetic model and the selection data and their comparison to the observed differences provide evidence of the appropriateness of the genetic models used for selection data.

## 3.4 Results and discussion

### 3.4.1 Descriptive statistics

Raw means and standard deviations of traits are shown in Table 3. 1 involving the entire data. Present results are similar to production levels reported in Spain for commercial farms and different maternal lines (Ramon and Rafel, 2002).

**Table 3. 1**Descriptive statistics (Mean, standard deviation (SD) and extreme values)for litter size traits (kids) and kindling interval (days).

| Trait | N | Mean | SD | Minimum | Maximum |
|---|---|---|---|---|---|
| Total born | 47132 | 9.80 | 3.07 | 1.00 | 26.00 |
| Number born alive | 47132 | 9.07 | 3.36 | 0.00 | 22.00 |
| Number weaned | 47097 | 7.79 | 3.05 | 0.00 | 18.00 |
| Number marketed | 43265 | 6.95 | 3.25 | 0.00 | 16.00 |
| Kindling interval | 34356 | 49.80 | 11.48 | 37.00 | 99.00 |

**N**: number of records

### Genetic parameters

Heritability estimates for litter size traits in A, V, H and LP lines were rather low and tended to decrease from birth to slaughter (Table 3. 2). The estimates were 0.14 for total born, 0.10 for number born alive, 0.08 for number weaned and 0.08 for number marketed. Heritability estimates for litter size traits vary considerably in the literature.Generally, the estimates are low to moderate. Some authors have reported estimates similar to ours (Rochambeau *et al.,* 1994; Sorensen *et al.,* 2001; García and Baselga, 2002a; Piles *et al.,* 2006). In contrast, other reports obtained lower estimates (Baselga *et al.,* 1992; Ferraz and Eler, 1996; Youssef *et al.,* 2008), while higher estimates have been reported for number born alive, number weaned and number marketed by García and Baselga (2002b) and for number born alive by Sánchez *et al.* (2006).

The estimates of the ratio of the permanent environmental variance to the phenotypic variance ($p^2$) for litter size traits in A, V, H and LP lines were low to moderate (Table 3. 2), but were very similar to estimates of heritability, which tended to decrease from birth and market time. Similar results were obtained by other authors (García and Baselga, 2002a, b; Al-Saef *et al.*, 2008).

**Table 3. 2**Genetic parameters of litter size traits and kindling interval.

| **Trait** | $h^2$ | $p^2$ | $r_g$ | $r_p$ | $r_e$ |
|---|---|---|---|---|---|
| Total born | 0.14±0.01 | 0.10±0.01 | 0.80±0.03 | 0.71±0.03 | 0.60±0.00 |
| Number born alive | 0.10±0.01 | 0.10±0.02 | 0.90± 0.01 | 0.83±0.02 | 0.81±0.00 |
| Number weaned | 0.08±0.01 | 0.08±0.01 | - | - | - |
| Number marketed | 0.08±0.01 | 0.07±0.01 | 0.96±0.01 | 0.94±0.01 | 0.91±0.00 |
| Kindling interval | 0.05±0.01 | 0.05±0.01 | -0.24±0.09 | 0.54±0.07 | -0.03±0.01 |

**$h^2$**: heritability, **$p^2$**: ratio of the permanent environmental variance to the phenotypic variance, **$r_g$**, **$r_p$** and$r_e$ : genetic, permanent and residual correlations between number weaned and trait, respectively.

Repeatabilities estimates (the sum of $h^2$ and $p^2$) were 0.24 for total born, 0.20 for number born alive, 0.16 for number weaned, and 0.15 for number marketed. Lukefahr and Hamilton (1997) and Sorensen *et al.* (2001) observed small $p^2$ values (not significantly different from zero) for litter size traits, except for litter size at weaning. Similarly, Ayyat *et al.* (1995) showed differences between heritability and repeatability estimates to be very small, reflecting the low importance of the permanent environmental and (or) non-additive genetic effects.

Genetic correlations between number weaned and other litter size traits were positive and high (0.80 to 0.96; Table 3. 2). The permanent environmental correlations between litter size at weaning and total born, number born alive and number at marketing were positive and high (0.71, 0.83, and 0.94, respectively; Table 3. 2). The same pattern was observed for the residual correlations. The present estimates of genetic correlations are in agreement with previous reports (Sorensen *et al.,* 2001; García and Baselga 2002a, b).

Kindling interval had low heritability (0.05), low $p^2$ (0.05) and low repeatability (0.10) as shown in Table 3. 2 Similar results were obtained by Baselga *et al.* (2003) for heritability, but the value of $p^2$ was 0.01. Khalil and Soliman (1989), Khalil (1993), and Moura *et al*. (2001) reported similar values of heritability. Low and negative genetic and residual correlations were obtained between kindling interval and litter size at weaning (-0.24 and -0.03, respectively; Table 3. 2), but the environmental permanent correlation was positive and moderate (0.54).

### 3.4.2 Contrasts between lines at their foundation

Table 3. 3 shows the contrasts employed between A, V, H and LP lines for litter size traits and kindling interval. Line V, at its foundation, was superior to line A for total born, number born alive, litter size at weaning and litter size at marketing (differences of 1.35, 1.24, 0.90 and 1.51 rabbits, respectively ($\alpha$=0.05)). The contrasts of lines H and LP relative to line A were significant and in favour of line H and line LP for litter size traits. Line LP had superior litter size trait values compared to line V. However, the results showed in Table 3. 3 have some apparent inconsistencies. For example, the contrast between lines A and Vfor total born was -1.35 rabbits and -1.07 between A and LP, but between V and LP was not 0.28 (1.35-1.07), it was -0.96. The explanation of these non-real inconsistencies is attributable to the different sets of farm-year-seasons and their interactions with the lines involved in the different contrasts.

Concerning interactions, certain situations occurred across the years at the UPV farm that could explain some of the farm-year-season x line interactions. Firstly, the spread of the enterocolitis disease affected a large period in the comparison between the lines A and H. The consequence of this disease was an increase in the post-weaning mortality, reducing the number of rabbits marketed. However, the sensitivity of the lines to enterocolitis was different, line A being the line most affected. Consequently, this event penalized line A in all line comparisons for number marketed. Secondly, there was a change in mating management that affected the lines V and LP from December 2003 to November 2005, which increased the period of restricted feeding by 2 weeks between weaning and the next parity. This restriction affected line V more than line LP (Theilgaard *et al*., 2007; Sánchez *et al*., 2008) because the line LP showed a better management in the body reserves, being consequently less affected by the temporal restriction of feeding (Theilgaard *et al*., 2007).

**Table 3. 3**Contrasts between the lines A, V, H and LP for litter size traits (rabbits/litter) and kindling interval (days).

| Trait | A - V | A - H | A - LP | V - H | V - LP |
|---|---|---|---|---|---|
| Total born | -1.35±0.04* | -1.76±0.16* | -1.07±0.08* | -0.09±0.19 | -0.96±0.08* |
| Number born alive | -1.24±0.04* | -1.25±0.17* | -1.11±0.09* | -0.02±0.19 | -1.32±0.08* |
| Number weaned | -0.90±0.04* | -0.75±0.17* | -0.87±0.11* | -0.32±0.19 | -0.96±0.10* |
| Number marketed | -1.51±0.05* | -0.93±0.16* | -0.73±0.13* | -0.29±0.17 | -0.97±0.11* |
| Kindling interval | 0.36±0.21 | 1.44±0.44* | 2.92±0.38* | 3.30±0.72* | 0.83±0.19* |

The contrast between lines H and LP was not possible because they did not share any farm-year-season;*: Significant difference at α = 0.05

At foundation, lines V, H and LP showed superiority over line A (Table 3. 3), which could be simply explained by the criteria used for their foundations. Lines V, H and LP were created by mating does and bucks of different origins from populations that had been subjected previously to selection for prolificacy. Line A was created by mating does and bucks of the New Zealand White breed (obtained from several commercial populations) that primarily maintained the standards of the breed more than selective improvement for productivity. In crossbreeding experiments in which direct genetic effects oflines were estimated for litter size traits, Orengo *et al*. (2003) showed superiority of line V over line A, and Baselga *et al*. (2003) also confirmed this superiority; however, the last authors did not find significant differences between line H and lines V and A.

Significant differences between lines for kindling interval were observed in all line comparisons, except between line A and V. The largest difference was 3.30 d for the comparison between line V and H, in favour of line H. More important differences were reported by Baselga *et al*. (2003) of 7.4 d in the comparison between the line A and V, and 6.5 d between line A and H, in favour of lines V and H, although the difference between line H and V was not significant (0.81 d). Cifre *et al*. (1998) did not finda significant difference in kindling interval between V line and H line of 1.02 d.

### 3.4.3 Contrasts between lines at fixed locations and times

Table 3. 4 presents the comparisons between the A, V and H lines for litter size traits and kindling interval from March 1997 to August 1998. Table 3. 5 shows the same contrasts between the A, V and LP lines, but from September 2007 to February 2009.

**Table 3. 4**The observed (Obs) and expected (Exp) contrasts between the lines A, V and H in terms of litter size traits (rabbits/litter) and kindling interval (days) from March 1997 to August 1998.

| Trait | Obs A - V | Exp A - V | Obs A - H | Exp A - H | Obs V - H | Exp V - H |
|---|---|---|---|---|---|---|
| Total born | -1.64±0.20* | -1.51 | -1.49±0.18* | -1.49 | 0.15±0.21 | 0.02 |
| Number born alive | -1.47±0.20* | -1.45 | -1.26±0.18* | -1.27 | 0.20±0.21 | 0.18 |
| Number weaned | -0.54±0.18* | -0.51 | -0.68±0.16* | -0.59 | -0.14±0.18 | -0.08 |
| Number marketed | -1.07±0.19* | -0.90 | -1.23±0.17* | -1.02 | -0.27±0.19 | -0.12 |
| Kindling interval | -3.32±0.63* | -2.55 | 1.30±0.74 | 0.82 | 4.62±0.70* | 3.37 |

*: Significant difference at α = 0.05

For the first period, the observed differences for litter size traits showed a clear pattern. Lines V and H showed superiority over line A, but did not show significant differences between them, which is contrary to results obtained by Cifre *et al*. (1998) who found a higher litter size for line H. Observed contrasts of lines V and H to line A were all significant over the average of line A with differences of 1.56 total born, 1.36 born alive, 0.61 weaned, and 1.15

marketed, which were consistently less than the other two lines. For kindling interval, the highest value was for the line V, being significantly different from lines A and H. The observed contrast between the latter two lines was non-significant and the average difference of these lines to the line V was 3.97 d, which is 8.1% higher of the normal kindling interval of 49 d.

The expected differences between A, V and H lines from March 1997 to August 1998 also appear in Table 3. 4, which shows values that are similar to the observed differences. This similarity possibly indicates the appropriateness of the models used to analyse the traits.

The observed differences from September 2007 to February 2009 (Table 3. 5), between lines A, V and LP show a very different picture than between lines A and V to the period from March 1997 to August 1998(Table 3. 4). The superiority exhibited by line V compared to line A was severely reduced for all litter size traits. The difference of 1.64 total born rabbits was reduced to 0.48, which was still significant, but the differences for number born alive, number marketed and kindling interval were very low.

The contrasts, between the line LP and the lines V and A, were not significant for any trait. Overall, it appears that lines A, V and LP showed similar present performances levels for reproduction traits. If the absolute values of the analysed traits were taken into account, the more important result would be the major improvement achieved in line A.

**Table 3. 5**The observed (Obs) and expected (Exp) contrasts between lines A, V and LP in terms of litter size traits (rabbits/litter) and kindling interval (days) from September 2007 to February 2009.

| Trait | Obs A - V | Exp A - V | Obs A - LP | Exp A - LP | Obs V - LP | Exp V - LP |
|---|---|---|---|---|---|---|
| Total born | -0.48±0.17* | -0.49 | -0.21±0.16 | -0.20 | 0.27±0.16 | 0.29 |
| Number born alive | -0.15±0.18 | -0.10 | -0.24±0.17 | -0.15 | -0.10±0.17 | -0.05 |
| Number weaned | -0.04±0.15 | -0.03 | -0.03±0.13 | 0.02 | 0.01±0.13 | 0.04 |
| Number marketed | -0.22±0.15 | -0.20 | -0.24±0.13 | -0.21 | -0.02±0.13 | -0.01 |
| Kindling interval | 0.56±0.71 | 0.79 | 0.69±0.70 | 2.34 | 0.13±0.65 | 1.55 |

*: significant difference at α = 0.05

Comparing the observed and expected differences (Table 3. 5) for this period, the same similarity, between both types of comparisons, was again observed. This similarity was strong for litter size traits, but for kindling interval was less, particularly between lines A and LP and between lines V and LP.

## 3.5 Conclusions

The current differences between the performances of the lines were lower than the differences at their origin. Reproductive performances of the four maternal lines (A, V, H and LP) were high and they appeared to be *a priori* as competitive lines to produce commercial crossbred does.

Important differences were detected between the lines at their origin, which can be explained based on the selection criteria used at the time of their foundation. Differences were also affected by interactions between farm-year-season and lines.

Strong agreement has been observed between the observed differences of the lines at fixed times and the expected differences that account for selection and the models used, especially for litter size traits, which served as an indicator of the appropriateness of these models.

## 3.6 Acknowledgements

This work was supported by the Spanish Research Projects (CICYT) AGL2008-03274 and ACOMP09 /013(Valencian Generality, Spain). The first author (Mohamed Ragab) appreciated the grant obtainedfrom the Mediterranean Agronomic Institute of Zaragoza (CIHEAM), Spain. Thanks are given to Prof. Steven Lukefahr for his critical revision of this manuscript.

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Chapter 4

# Effective population size and inbreeding depression on litter size in rabbits. A case study

## 4.1 Abstract

The purpose of this study is to use demographic and litter size data of four Spanish maternal lines of rabbits (A, V, H and LP), as a case study, in order to: i) estimate the effective population size of the lines, as a measure of the rate of increase of inbreeding and ii) study if the inbreeding effect on litter size traits depends on the pattern of its accumulation over time. The lines are being selected for litter size at weaning, kept closed at the same nucleus of selection under the same program of selection and management. The study considered 41, 36, 10 and 6 generations of the respective lines, 47,794 litters and a pedigree of 14,622 animals.

Some practices in mating and selection management, such as avoiding the matings between animals sharing grandparents and making that each sire contributed with a son to the next generation,allow an increase of the inbreeding coefficient lower than 0.01 per generation in these lines of around 25 males and 125 females. The effective population size (Ne) for them was around 57.3, showing that the effect of selection, increasing the inbreeding has been counterbalanced by the management practices, trying to reduce the rate of inbreeding increase.

The inbreeding of each individual was partitioned in three components: old inbreeding (inbreeding accumulated between the foundation of the line and generation 15th for animals born after generation 30th), intermediate (inbreeding accumulated between generations 15th to 30th for animals born after generation 30th or the inbreeding accumulated in the first 15generation for animals born before generation 30th) and new (the rest of situations).

The coefficients of regression of the old, intermediate and new inbreeding on total born (TB), number born alive (NBA) and number weaned (NW) per litter, showed a decreasing trend from positive to negative values. Regression coefficients significantly different from zero were the ones for the old inbreeding on TB (6.79±2.37) and NBA (5.92±2.37). The contrast between the coefficients of regression between the old and new inbreeding were significant for the three litter size traits: 7.57±1.72 for TB; 6.66±1.73 for NBA and 5.13±1.67 for NW. These results have been interpreted as the combined action of the purging of unfavourable genes and artificial selection favoured by the inbreeding along the generations of selection through the increase thefrequency of homozygotes.

**Key words:** inbreeding,litter size, new inbreeding, old inbreeding, purging, selection.

## 4.2 Introduction

The rabbit lines used in crossbreeding schemes for meat production are small and closed populations submitted to within line selection for generations (Garreau *et al*., 2004; Baselga, 2004). Due to their finite population size and selection, the inbreeding accumulates along the generations and it is common to take measures to reduce its rate of increase. Inbreeding is the result of mating between relatives and implies an increase of expected homozygosis within the populations (Falconer and Mackay, 1996). Inbreeding negatively affects the means of the traits and an increased risk to a breeding program in terms of the variance of genetic gain (Meuwissen, 1991).

It is known that time and selection, natural or artificial, can diminish the depressive effect of the inbreeding, due to a reduction of the frequency of unfavorable alleles, genetic purging, and the consequent reduction of the genetic load (Templeton and Read, 1984; Lacy and Ballou, 1998).

In previous studies, estimating the rate of genetic purging, it was observed that inbreeding depression was reduced after long time and this reduction was constant, i.e. it depends more on inbreeding recently generated than on old accumulated inbreeding (Parland *et al*., 2009; Gulisija and Crow, 2007; Hinrichs *et al*., 2007). The new inbreeding could take into account the impact of newly arisen mutations, whereas old unfavorable alleles could have diminished their frequency and, sometimes, left the population.

In Spain there are several maternal lines of rabbits (Ragab and Baselga, 2011), founded between 1980 and 2004, some of them with a long history of selection for litter size at weaning, housed together in the same nucleus and submitted to the same program of selection and management. They are material of interest to analyze, as a case study, the effect of the measures that intend to control the inbreeding increase rate and the different effect of the inbreeding on the litter size traits, depending on the time of its production, old or recent. Consequently, the purpose of this article is to use pedigree and litter size data of those lines in order to study several items related to inbreeding: i) estimate the effective population size of the lines, as a measure of the rate of increase of inbreeding and ii) study if the inbreeding effect on litter size traits depends on the pattern of its accumulation over time.

## 4.3 Materials and Methods

### *4.3.1 Animals and traits*

The animals in the present study were from four maternal lines of rabbits (A, V, H and LP) selected for litter size at weaning. The analysis included data from the 1st generation of selection to the generation 41st in A line, 37th in V line, 10th in H line and 6th in LP line. All lines were kept closed since its foundation.

Line A was founded in 1980 sampling New Zealand White (NZW) rabbits and has been selected using a family index (Estany *et al*., 1989). Line V was founded in 1982 as a synthetic line of four specialised maternal lines. This line has been selected using BLUP under an animal-repeatability model (Estany *et al*., 1989), as the lines H and LP. Line H was founded applying a hyperprolific selection scheme (Cifre *et al*., 1998). The LP line was founded by selecting females from commercial farms that showed extremely high productive lives with prolificacy near or above the average of the Spanish commercial rabbit population (Sánchez *et al*., 2008). Selection was done in non-overlapping generations and the does for the next generation were selected from the best evaluated matings. It was tried to avoid the mating between close relatives, i.e. mates could not have common grandparents. The bucks were selected within sire from its best mating, trying that each sire contributed with a son to the next generation.

The litter traits studied were: total born (TB), number born alive (NBA) and number at weaning (NW, 28 d).

### 4.3.2 Inbreeding computation

Inbreeding ($F_u^t$) for an animal born in generation u, taking as base generation the generation t (t<u), was computed using a modified version of the recursive algorithm proposed by Aguilar and Misztal (2008). The modification consists in saving those relationship coefficients that are computed when obtaining each inbreeding coefficient, thus no recalculation are needed and the method can be better applied to deep pedigrees. When t=0 the inbreeding computed is the total inbreeding accumulated in the animal from the foundation of the line (F).

### 4.3.3 Partition of inbreeding (old, intermediate and new)

First we define $F_u^t$ as the inbreeding of an animal pertaining to generation u, when the generation t is considered as the base generation (t<u).For an animal pertaining to generation u and given two generations, t1 and t2, such that

0<t1<t2<u, we are going to decompose $F_u^0$ into three components: the inbreeding accumulated until generation t1 ( $F_{0,t1}^0$ ), the inbreeding accumulated from t1 to t2 ( $F_{t1,t2}^0$ ) and the inbreeding accumulated from t2 to u ( $F_{t2,u}^0$ ). These components can be computed using the equation for inbreeding in hierarchically structured populations (Wright, 1922), for i=1, 2:

$1-F_u^0=\left(1-F_{0,ti}^0\right)\left(1-F_u^{ti}\right)$, thus

$F_{0,ti}^0=\dfrac{F_u^0-F_u^{ti}}{1-F_u^{ti}}$, and

$F_{ti,u}^0=F_u^0-F_{0,ti}^0=(1-F_{0,ti}^0)F_u^{ti}$

The last formula shows how $F_u^{ti}$ is scaled by the factor $(1-F_{0,ti}^0)$ to give $F_{ti,u}^0$

Correspondingly, the part of $F_u^0$ accumulated between generations t1 and t2, will be,

$$F_{t1,t2}^0=F_{t1,u}^0-F_{t2,u}^0=F_{0,t2}^0-F_{0,t1}^0$$

For an animal born after generation t2, $F_{0,t1}^0$, $F_{t1,t2}^0$ and $F_{t2,u}^0$ were computed. To simplify notation they will be named, $F_{old}$, $F_{\text{int}}$ and $F_{new}$, respectively. For an animal born between generations t1 and t2 only $F_{\text{int}}$ and $F_{new}$ can be computed, as $F_{0,t1}^0$ and $F_{t1,u}^0$, and $F_{old}$ is set to 0. For an animal born before generation t1only $F_{new}$ was computed, as $F_u^0$, and $F_{old}$, $F_{\text{int}}$ set to 0.The analysis shown in this article, corresponds to t1=15 and t2=30.

### 4.3.4 Effective population size

Naming $\overline{F}_u$ the average of inbreeding of the individuals of the last generation of a line, and $N_e$ the effective population size of the line from foundation to the current generation (u), the formula that relates both is,

$\overline{F_u}=1-\left[1-\dfrac{1}{2N_e}\right]^u$, this formula can be used to compute $N_e$, (Crow and Kimura, 1970).

Along generations, the number of males ( $N_{mi}$ , for generation i) and females ( $N_{fi}$ , for generation i) effectively contributing progeny to the next generation was known and we could compute an equivalent population size, as if this number would be constant and no selection, random mating and equal probability of giving progeny to the next generation had performed. This equivalent population size was named $N_{ec}$ , this number was computed for the period from the foundation of each line to the last generation considered, as follows:

$$\frac{1}{N_{ec}} = \frac{1}{u}\sum_{i=1}^{u}\frac{1}{N_{ei}} \text{ , being } \frac{1}{N_{ei}} = \frac{1}{4N_{mi}} + \frac{1}{4N_{fi}} \text{ , (Crow and Kimura, 1970)}$$

A comparison between $N_e$ (computed from the observed inbreeding coefficients) and $N_{ec}$ (computed from the number of sires and dams) was made to discuss the importance of the hypothesis assumed when computing $N_{ec}$ .

### *4.3.5 The effect of old, intermediate and new inbreeding on litter traits.*

The model used for the trait t (t= TB, NBA, NW) was:

$$Y_{tjiknl} = PS_{tj} + L_{tk} + YSL_{tik} + \pi_t F_{kn,old} + \alpha_t F_{kn,int} + \gamma_t F_{kn,new} + a_{tkn} + p_{tkn} + e_{tjiknl}$$

where, $y_{tjiknl}$ is the $l$record of the trait $t$ corresponding to the doe $n$, nested within the line $k$, obtained at physiological state $j$, year season $i$ ; $PS_{tj}$ is the fixed effect of the physiological state of the doe (5 levels, depending on the parity order and lactation state at the moment of positive insemination: 1 for nulliparous, 2 (4) for primiparous lactating (no lactating), 3 (5) for multiparous lactating (no lactating) does,); $L_{\mathrm{tk}}$ is the fixed effect of the line (4 levels); $YSL_{\mathrm{tik}}$is the fixed effect of the year-season-line combination; $\alpha_{t,}$ $\gamma_t$and$\pi_t$are regression coefficients of old ($F_{old}$), intermediate ($F_{int}$) and new inbreeding coefficients ($F_{new}$),respectively; $a_{\mathrm{tkn}}$ ($p_{\mathrm{tkn}}$) is a random effect of the additive genetic value (permanent environmental effect) of the doe and $e_{\mathrm{tjiknl}}$ is the residual. In order to take into account the effect of selection for NW and avoid biased estimates (Sorensen and Johansson, 1992), two-trait models, including NW, were used for the analysis of TB and NBA. The models were solved using variance components obtained by Ragab and Baselga (2011) for the same set of data. Contrast between the coefficients of regression of the old, intermediate and new inbreeding were performed and significance was claimed at a first type error, $\alpha$=0.05.

A total of 47,794 parities were analysed (16,979, 21,640, 4,143 and 5,032 parities for A, V, H and LP, respectively). The pedigree file included 14,622 individuals. All analyses were undertaken using blupf90 family program (Misztal *et al.*, 2002).

## 4.4 Results and discussion

### *4.4.1 The effective population size.*

The last generation considered for A,V, H and LP lines was, respectively, the41st, 36th, 10th and 6th, and the average inbreeding reached in these generations was 0.31, 0.26, 0.08 and 0.04. Figure 1 shows the pattern of inbreeding accumulation along generations. The computations of effective population size have been done, exclusively for the first three lines, because the number of generations of line LP is too small. It must be taken into account that the effect of avoiding the mating between animals sharing grandparents is that the inbreeding is 0 for all animals of the first four generations, and in line LP the last generation is the sixth.

The resulting values of $N_e$ were: 53 animals for line A, 58 animals for line V and 54 animals for line H. The corresponding values for $N_{ec}$ were: 59 animals for line A, 60 animals for line V and 58 animals for line H. Figure 2 presents the values of $N_{ei}$, computed from the number of sires and dams which contributed progeny to the next generation for each line, that were used for computing $N_{ec}$.

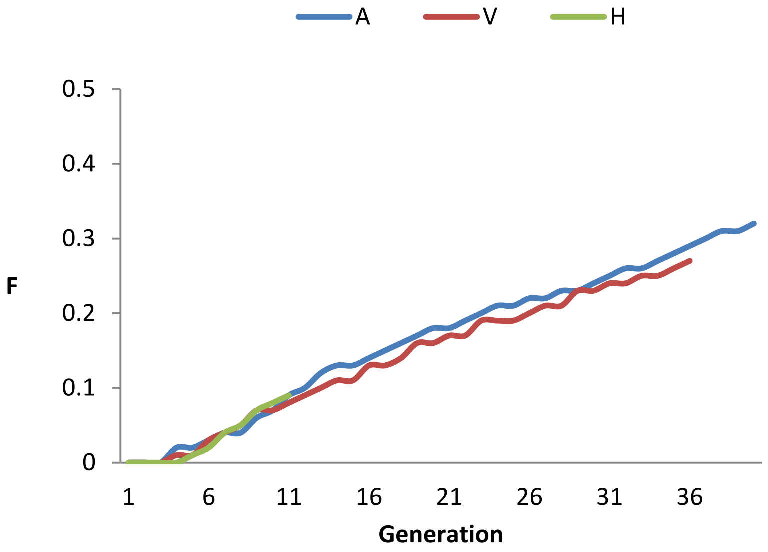

**Figure 4. 1**The pattern of inbreeding accumulation (F) along generations for each line.

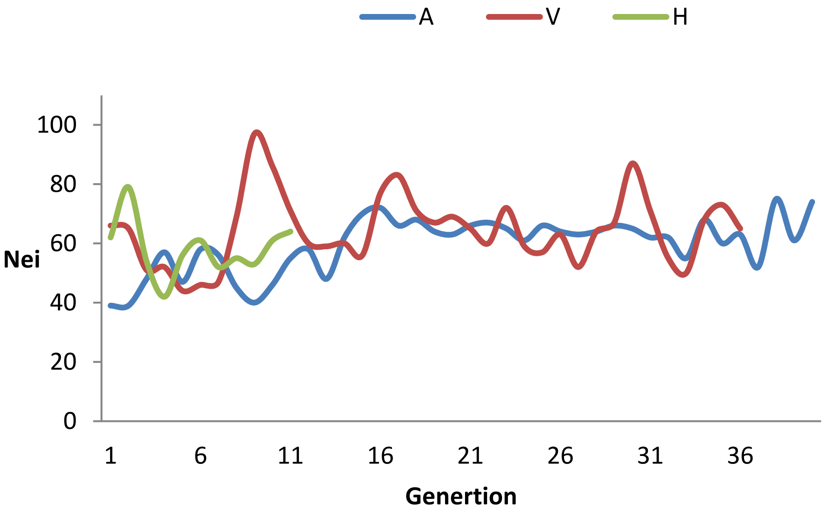

**Figure 4. 2**The value of $N_{ei}$, computed from the number of sires and dams with contributed progeny, for line and generation.

It was not expected that these values were close to the $N_e$ values, because the assumptions made to compute $N_{ec}$ are, actually, not met. However, they are quite similar. It means that the differences expected between the two values, due to the effect of selection, equal probability contribution and random mating compensate between them. Thus, no considering selection when computing $N_{ec}$ would mean that the expected value of $N_{ec}$ should be higher than $N_e$ because the selection effect leads to increase the inbreeding, reducing the effective population size (Wray and Thompson, 1990). However, the animals actually contributing to the progeny of the next generation have a contribution more similar than if the assumption of equal probability would be met, particularly in the via sire to son where is forced that each sire contribute with a son to the next generation. The consequence is that $N_{ec}$ should be lower than $N_e$ (Caballero, 1994). Finally, the mating management for avoiding mating of animals sharing grandparents would have the effect of reducing the increase of inbreeding compared to random mating and consequently it would be expected an $N_{ec}$ lower than $N_e$. The summary is that the selection effects to increase inbreeding are counterbalanced by the opposite effects of avoiding matings between close relatives and the similarity of contributions to the next generation of the animals that actually contribute.

### *4.4.2 The effect of the old, intermediate and new inbreeding.*

In this section the interest is to differentiate the effects of the old ($F_{old}$), intermediate ($F_{int}$) and new ($F_{new}$) inbreeding on litter size traits. A colinearity between them will prevent this differentiation, but the correlations computed between them are negligible between new and intermediate inbreeding (0.08) and between old and intermediate inbreeding (0.13) and weak between new and old inbreeding (0.29) in absolute value. It means that the effects estimated for each type of inbreeding will have low error covariances between them and could be really attributed to the corresponding type.Table 4. 1 shows the estimated regression coefficients for $F_{old}$, $F_{int}$ and $F_{new}$*as* well as their contrasts. Both old and intermediate inbreeding had positive estimates on all litter size traits, being only significant the effect of old inbreeding on the total born and number born alive. A decreasing trend, from positive to negative values, can be noted in the regression coefficients from the old to the new inbreeding. The effect of new inbreeding was always negative, but it has not been possible to prove that is significantly different of zero due to the high standard errors of the estimates.

In general, the contrasts between old and the other types of inbreeding were positive and significant favouring old inbreeding, while the contrasts between intermediate and new inbreeding were positive but non-significant.

**Table 4. 1**Regression coefficients of old ($F_{old}$), intermediate ($F_{int}$) and new ($F_{new}$) inbreeding on litter size traits (kids) and their contrasts.

| Inbreeding type | Total born | Number born alive | Number weaned |
|---|---|---|---|
| $F_{old}$ | 6.79±2.37* | 5.92±2.37* | 3.70±2.25 |
| $F_{int}$ | 1.51±2.45 | 0.92±2.45 | 2.17±2.37 |
| $F_{new}$ | -0.78±1.85 | -0.73±1.85 | -1.43±1.75 |
| $F_{old}$ vs $F_{int}$ | 5.28±1.79* | 4.99±1.79* | 1.53±1.73 |
| $F_{old}$ vs $F_{new}$ | 7.57±1.72* | 6.66±1.73* | 5.13±1.67* |
| $F_{int}$ vs $F_{new}$ | 2.28±2.03 | 1.66±2.03 | 3.60±2.02 |

$^{*}$: Significant difference at α = 0.05

Similar results were found in mice by Hinrichs *et al*. (2007) and in Irish Holstein-Friesians by Parland *et al*. (2009). They found that new inbreeding is the major responsible of inbreeding depression.

The positive estimates obtained for the regression coefficients of the old inbreeding and its evolution to negative values for the corresponding estimates of the new inbreeding can be explained invoking the purging of the worst alleles affecting the litter size traits potentiated by the artificial selection for litter size at weaning.Under directional dominance, but non over-dominance, the genetic values of the heterozygotes are between the values of the homozygotes and over their mean.The process of accumulating inbreeding for a long number of generations increases the frequency of homozygotes. If they correspond to undesirable alleles it gives opportunities for purging (Gulisija and Crow, 2007), while if the homozygotes are of favourable alleles, natural and artificial selection will favour their transmission to the next generation, increasing the averages of the traits in both cases. Thus this process could convert the old inbreeding in beneficial, explaining the positive values of the coefficient of regression on old inbreeding, the negative values for the new inbreeding and the intermediate values for the intermediate inbreeding. In the analysis of Hinrichs *et al*. (2007) in mice, the regression coefficients on new inbreeding were always negative but for old inbreeding became positive when the number of generations associated to old inbreeding were the generations before the last 20.

Ferraz *et al*. (1991) and Moura *et al*. (2000) in rabbits have previously estimated negative effects of inbreeding on prolificacy traits that could be compared to the regressions coefficients for new inbreeding obtained in this study. Moura *et al.* (2000) estimated a reduction of 0.81 and 0.59 rabbits per litter at birth and at weaning, respectively, caused by an increase of 0.1 in the inbreeding of the doe, and Ferraz *et al*. (1991) found a drop of 1.4 weaned rabbits per litter when the inbreeding coefficient increases the same magnitude; this effect was 26% of the mean of the trait. These effects are considerably higher than the ones reported in this study. Values of inbreeding depression of this magnitude had masked the response to selection estimated in the lines V and A, response that had proved (García and Baselga, 2002a, b). Similarly, when crossbred does between different generations of line A and V were compared (Costa *et al*., 2004; Quevedo *et al*., 2005), the differences were, only, a little higher than expected from the intra-line response to selection. This result was explained by the recovery of the inbreeding depression in the crossbred does. All these results seem to show that in the lines studied here the depressing effect of the new inbreeding is lower than in the populations studied by Ferraz *et al*. (1991) and Moura *et al*. (2000).

## 4.5 **Conclusions**

The effects of selection to increase inbreeding can be counterbalanced by the opposite effects of avoiding matings between close relatives and the similarity of contributions to the next generation of the animals that actually contribute.

The effects of old, intermediate and new inbreeding on litter size traits change from positive, for old inbreeding, to negative for new inbreeding and values in between them for intermediate inbreeding, due to a combined result of the purging of unfavourable genes and artificial selection.

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Chapter 5

# Litter size components in a diallel cross of four maternal lines of rabbits

## 5.1 Abstract

A crossbreeding experiment between four maternal lines of rabbits was carried out to estimate crossbreeding effects on litter size components. The experiment was designed as a complete diallel cross involving four lines selected for litter size at weaning (A, V, H and LP) and their twelve simple crosses. Does from these sixteen genetic groups were distributed in four Spanish farms but only V line was present in all farms allowing the connectivity of the data. A total of 2,025 does in the third, fourth or fifth gestations, were subjected to laparoscopy. The recorded traits were ovulation rate (**OR**), number of implanted embryos (**IE**), total born (**TB**), embryo survival (**ES**), foetal survival (**FS**) and prenatal survival (**PS**). Components of variance were estimated using an animal model with a REML procedure. The differences in direct genetic effects, maternal genetic effects and individual heterosis between the lines were estimated according to Dickerson model after solving the appropriate animal model conditioned on the REML variance components.

It should be noted the high values obtained for the mean of all traits compared to the ones obtained in previous studies. The differences between the performances of the line groups were important. Although line A showed lower OR than the other lines, differences in OR and IE between genotypes were not significant. Differences between A line and the other lines were relevant for TB, (more than 1 kid).

Regarding differences between crossbred groups and V line, only significant differences were observed in favour of HV with respect to V line for OR (1.03 ova) and in favour of AH for IE (1.07 embryos).

Regarding TB, the obtained differences were important in two cases: favourable in the case of AH and unfavourable in the case of LV (-1.33 rabbits). Important and significant reciprocal effects were found in some cases, especially for OR in the crosses AL and LA (-2.00 ova) and in the crosses AV and VA for TB (-1.75 kids). Regarding direct genetic effects line LP presented higher estimates than the other lines, but being only significantly different with A line (2.01 ova for OR and 2.13 kits for TB).The maternal effects were significant only for some contrasts in OR and revealed that the LP line was inferior to the others (1.25 ova respect to the A line, 1.01 respect to the H line and 0.91 respect to the V line). High positive values for heterosis effect were found between lines A and H (1.16 ova for OR, 1.46 embryos for IE and 1.44 kids for TB). The cross between lines LP and V had a negative heterosis for all traits with a high value for TB (-1.70 kids).

**Key words:** crossbreeding components, maternal lines, ovulation rate, litter size, rabbits, prenatal survival.

## 5.2 Introduction

Litter size is a very important trait in maternal lines of rabbits (García-Ximenez *et al.,* 1996; Gómez *et al.,* 1996) and, consequently, the study of its components has interest in order have a better understanding of the nature of the genetic control of litter size. Litter size is limited by the number of ova produced and depends on fertilization rate, and pre- and post-implantation embryonic mortality. Prenatal mortality is around 30 % in rabbits (García and Baselga, 2002; Mocé *et al*., 2010). Several studies have been carried out in order to interpret the observed heterosis in litter size traits in prolific mammals which could be a consequence of the superiority of the crossbreds in ovulation rate or in embryo survival, or both (Bradford and Nott, 1969). Some crossbreeding studies have considered litter size, but few of them have dealt with its components.

In rabbits, Hulot and Matheron (1979) detected positive and significant heterosis ranged from 6.7 to 13.8% andfrom10.6 to 19.4%for ovulation rateand prenatal survival, respectively. In another study, Brun *et al*. (1992) observedfrom 4.4 to 7.4%positive andin some cases significant heterosis for ovulation rateand 6.3% for prenatal survival,whereas this was not foundfor ovulation rate in pigs (Bidanel *et al*., 1990 and Galvin *et al*., 1993). Additionally, Haley and Lee (1990) concluded that the high level of prenatal survival at a given ovulation rate was mainly controlled by maternal genes whereas the embryo has little influence. In mice, Falconer and Roberts (1960) found directional dominance of genes affecting ovulation rate and pre-implantation losses when they crossed inbred lines. However, post-implantation losses were mainly affected by the additive effect of the genes. Davis and Lamberson (1991) reported that the genetic group significantly affectedthe ovulation rate and the total number of foetuses, but not the total number of implantations.

The main objective of this study was to analyse the litter size components in a diallel cross between four maternal lines that allows the comparison between the lines and their simple crosses, as well as to estimate the direct and maternal effects associated to the lines, and the heterosis associated to the crosses.

## 5.3 Materials and Methods

### *5.3.1 Animals and Management*

A complete diallel cross involving four maternal lines of rabbits: A, V, H and LP, selected for litter size at weaning was carried out. Their current generation of selection was 41st, 37th, 20th and 7th, respectively (see details of the lines in section 1. 10). Data were collected from January 2009 to October 2011.

The experimental work was carried out in four Spanish farms with a total of 2,260 cages available for breeding animals. The farms were located in León (farm 1, 800 does), Castellón (farm 2, 800 does), Tarragona (farm 3, 300 does) and finally the farm of Universidad Politécnica de Valencia (UPV) (farm 4, 360 does). The genetic groups involved in the experiment were the 4 lines (AA, VV, HH and LL) and the 12 single crosses (AV, VA, AH, HA, AL, LA, VH, HV, VL, LV, HL and LH). Notice that first letter refers to the sire line and the second to the dam line and L is used to identify the LP line. All the crossbreds and V line animals were raised in farms 1 and 2; females of the groups VV and HH were raised in the farm 3 and VV, AA and LL animals were raised in farm 4. The group VV was used as the reference line because it was present in all the farms, allowing the connectivity of the data among farms, assuming no interaction between farm and line.

Management of the animals slightly differed across farms. In farm 1 and 2, the mating was performed every 42 days, whereas in farms 3 and 4 weekly mating was performed. In all farms, the first mating was around 18 weeks of age for males and females. Natural mating was used in farm 3 and 4 while artificial insemination was conducted in farms 1 and 2. The does were served 10-12 days post-kindling and a pregnancy test was carried out by abdominal palpation on day 12 after mating. In farm 1 and 2, does were inseminated with semen coming from a paternal line (10-20x$10^6$ spermatozoa per dose) with a prior injection of gonadotropin to induce the ovulation (20 U.I.).The semen was collected 16 hours before insemination.

Rabbits fed *ad libitum* on a standard commercial pelleted diet. Does were under a constant photoperiod of 16: 8 h.

### *5.3.2 Traits and Statistical analyses*

The studied traits were ovulation rate (**OR**; estimated as the number of corpus luteum in both ovaries), number of implanted embryos (**IE**; measured as the number of implantation sites), total born (**TB**; measured as the total born per litter), embryo survival (**ES**; estimated as IE / OR), fetal survival (**FS**; estimated as TB / IE), and prenatal survival (**PS**; estimated as TB / OR). Records were obtained from does in their third or fourth or fifth gestations that were subjected to a laparoscopy, only once, 11-12 days after mating following the surgical technique described by Santacreu *et al*. (1990). The laparoscopy was done only one time per doe.Laparoscopic surgery is minimally invasive, performed after inflating the abdomen with gas, usually carbon dioxide, which creates a space between the wall of the abdomen and the organs inside. Using short incisions in the skin, narrow tubes are inserted into the abdominal wall so that instruments can be passed through them to perform the manoeuvres necessary for the operation. All this is viewed directly on a video monitor, which receives its picture from a video camera attached to the laparoscope (Figure I. 2).

All traits were analysed using the following mixed model:

$$Y_{ijkl} = GFYS_i + PO_j + L_k + a_l + e_{ijkl}$$

where $Y_{ijkl}$ corresponds to the record of the $l$ doe, obtained at the genetic group- farm year season $i$, parity order $j$ and physiological state $k$; $GFYS_i$ is the fixed effect resulting from the combination of the genetic group and farm-year-season (129 levels: for $i$= 1, …, 129); $PO_j$isthe parity order (3 levels : for $j$ = 3, 4 and 5); $L_k$ is the effect of lactation state of the doe (2 levels: lactating does and not lactating does at mating time : for $k$ = 1 and 2); $a_l$is the random additive genetic value of the doe at which the observation corresponds ( for $l$ = 1, …, 2025), and $e_{ijkl}$ is the residual. In a previous step, the variance components of the random effects were estimated by REML, using the remlf90 program (Misztal *et al*., 2002). Given the previously estimated variance components, the model was solved by BLUP, using the blupf90 program (Misztal *et al*., 2002) to obtain the model estimates, as well as their (co)variance matrix and the differences between all genetic groups and the VV groups. From these contrasts and its variance covariance matrix the differences between direct genetic effects of the lines, the differences between maternal genetic effects of the lines and the individual heterosis of the crosses were estimated according to the model of Dickerson (1969).

## 5.4 Results and Discussion

Means and standard deviations of the considered traits are presented in Table 5. 1. The mean of OR is similar to the values obtained by other authors in selection experiments for uterine capacity or for OR (Santacreu *et al*., 2005;Ibáñez-Escriche *et al*., 2006; Laborda *et al*., 2011, 2012) whereas higher means were obtained for the other traits.

**Table 5. 1**Descriptive statistics of the experimental data.

| **Traits**[1] | **N** | **Mean** | **Minimum** | **Maximum** | **SD** |
|---|---|---|---|---|---|
| OR[1] | 2024 | 15.30 | 6.00 | 30.00 | 2.79 |
| IE[1] | 2024 | 13.28 | 1.00 | 27.00 | 3.11 |
| TB[1] | 1856 | 11.03 | 1.00 | 22.00 | 3.32 |
| ES[1] | 2024 | 0.87 | 0.06 | 1.00 | 0.16 |
| FS[1] | 1856 | 0.84 | 0.11 | 1.00 | 0.18 |
| PS[1] | 1856 | 0.73 | 0.56 | 1.00 | 0.21 |

[1] OR=ovulation rate; IE=implanted embryos; TB=total born; ES = embryo survival; FS = fetal survival; PS= prenatal survival.

Heritability estimates were 0.24, 0.10, 0.12, 0.07, 0.06 and 0.13 for OR, IE, TB, ES, FS and SP, respectively. García and Baselga (2002), *Bolet et al.* (1994), Blasco *et al.* (1993), Piles *et al.*(2006) and Laborda *et al.* (2011, 2012)reported similar estimates of heritability for OR, EI, TB, ES and SP. In contrastBlasco *et al.* (1993), Ibáñez *et al.* (2006) and Laborda *et al.*(2012) reported higher estimates for FS. The heritability of PS was in agreement with the estimates in pigs (Johnson *et al.,* 1999; Rosendo *et al.,* 2007) and mice (Clutter *et al.,* 1990).

The differences between the line groups are given in Table 5. 2. These figures show that some differences between lines are important from the view point of rabbit production. For example, the differences in TB between A line and other lines were more than 1.15 rabbits per litter. Differences in OR and IE between lines were not significant. Regarding TB, A line had 1.15, 1.68 and 1.38 less rabbits than V, LP and H lines, respectively. These differences were due to an outbreak of colitis that affected farm 4 from the December 2010 to the end of the experiment in October 2011. The sensitivity of the lines to the colitis was different; being A line the most affected one. This disease provoked a decrease in the fetal survival, a reduction of the number of total born and increased the mortality at birth as well. The differences between lines LP, H and V regarding OR, IE and TB, were not significant.

Regarding the embryo, fetal and prenatal survival, the lines did not show significant differences.

**Table 5. 2**Contrasts (standard errors) between line groups for litter size components.

| | OR[1] | IE[1] | TB[1] | ES[1] | FS[1] | PS[1] |
|---|---|---|---|---|---|---|
| AA-HH | -1.30(0.76) | -0.28(0.87) | -1.38(0.97) | 0.06(0.05) | -0.06(0.06) | -0.00(0.06) |
| AA-LL | -0.80(0.64) | -0.69(0.78) | -1.68(0.83)* | 0.01(0.05) | -0.08(0.05) | -0.05(0.05) |
| AA-VV | -1.00(0.57) | -0.52(0.67) | -1.15(0.76) | 0.04(0.04) | -0.03(0.05) | -0.01(0.04) |
| HH-VV | 0.29(0.50) | -0.23(0.56) | 0.24(0.60) | -0.02(0.03) | 0.03(0.04) | 0.01(0.03) |
| LL-HH | -0.49(0.71) | 0.41(0.81) | 0.30(0.84) | 0.05(0.05) | 0.02(0.05) | 0.04(0.05) |
| LL-VV | -0.20(0.51) | 0.17(0.59) | 0.53(0.60) | 0.02(0.04) | 0.05(0.04) | 0.05(0.04) |

[1]OR=ovulation rate; IE=implanted embryos; TB=total born; ES = embryo survival; FS = foetal survival; PS= prenatal survival; L:LP line; * significant difference (α=0.05).

The differences between crossbred groups and V line are presented in Table 5. 3. Concerning OR, only HV showed a significant difference with respect to V line. The standard errors of the estimates would permit to detect differences of around 6% of the OR mean or higher, but in the majority of the cases they have been lower than the 5%. The difference estimated for OR between all crossbreds and V line was around 2 % of the mean. Referring IE, difference around 9 % of the mean or higher could have been detected as significant. Only the group AH showed a significant difference with respect to the V line, and the corresponding contrast for all the crossbreds was 3% of the mean.

**Table 5. 3**Contrasts (standard errors) between crossbred groups[1] and V line.

| | OR[2] | IE[2] | TB[2] | ES[2] | FS[2] | PS[2] |
|---|---|---|---|---|---|---|
| AH-VV | 0.78(0.45) | 1.07*(0.51) | 0.91(0.49) | 0.02(0.05) | 0.01(0.03) | 0.04(0.03) |
| AL-VV | -0.30(0.49) | 0.40(0.56) | -0.57(0.53) | 0.03(0.06) | -0.05(0.03) | -0.01(0.03) |
| AV-VV | 0.25(0.40) | 0.67(0.47) | 0.16(0.45) | 0.03(0.04) | -0.02(0.03) | 0.01(0.03) |
| HV-VV | 1.03(0.43)* | 0.86(0.49) | 0.54(0.47) | -0.02(0.05) | 0.00(0.03) | -0.00(0.03) |
| LH-VV | 0.63(0.40) | 0.31(0.44) | -0.08(0.46) | -0.03(0.05) | -0.01(0.03) | -0.03(0.03) |
| LV-VV | -0.44(0.38) | -0.37(0.46) | -1.38(0.39)* | -0.02(0.04) | -0.05(0.02)* | -0.06*(0.02) |
| All-VV | 0.32(0.30) | 0.49(0.33) | -0.07(0.33) | 0.00(0.03) | -0.02(0.02) | -0.01(0.02) |

[1] One cross and its reciprocal were considered together. [2]OR=ovulation rate; IE=implanted embryos; TB=total born; ES = embryo survival; FS = foetal survival; PS= prenatal survival; All=Average of all crossbred; L:LP line; *significant difference (α=0.05).

The results regarding to TB showed that the obtained differences with line V were significantly unfavourable to LV group. The inferiority of LV was due to a significantly lower fetal and prenatal survival. When the average of all crossbreds was compared with V line, the magnitude of the contrast was always lower than the 3% of the corresponding means and no significant differences were found for any of the traits.

The importance of using a particular line either as sire or dam in a cross was assessed by checking the differences between a particular cross and their reciprocal. Differences between reciprocal crosses reflect differences in gene frequencies between lines for the additive maternal and dominance maternal effects (Eisen *et al.,* 1983). Some relevant differences between reciprocal crosses were observed (Table 5. 4) but due to the large sampling errors of the estimates, few significant differences were found. However, some values are important in rabbit production, as it has been commented before.

For the crosses AL and LA it would be preferable to use the A line as the dam because a superiority is shown for OR. The cross VA has got significant and better results than its reciprocal in TB and PS. These results are indicators that A line can have positive maternal effects. The reciprocal crosses between A and H lines did not differ from each other in any of the analysed traits.

**Table 5. 4**Contrasts (standard errors) between reciprocal crosses for litter size components.

| | **OR**[1] | **IE**[1] | **TB**[1] | **ES**[1] | **FS**[1] | **PS**[1] |
|---|---|---|---|---|---|---|
| AH-HA | 0.79(0.66) | 0.42(0.80) | 0.72(0.79) | -0.02(0.05) | 0.03(0.05) | 0.01(0.05) |
| AL-LA | -2.00(0.71)* | -1.33(0.89) | -0.33(0.84) | 0.02(0.06) | 0.03(0.05) | 0.06(0.05) |
| AV-VA | -0.62(0.62) | -0.46(0.77) | -1.75(0.74)* | -0.01(0.05) | -0.09(0.05) | -0.09*(0.04) |
| HV-VH | 0.98(0.58) | 0.83(0.71) | 0.78(0.70) | 0.00(0.04) | 0.00(0.04) | -0.00(0.04) |
| LH-HL | 1.33(0.51)* | 0.60(0.60) | 0.84(0.72) | -0.03(0.04) | 0.02(0.05) | 0.01(0.04) |
| LV-VL | -0.09(0.63) | 1.04(0.79) | -0.73(0.66) | 0.07(0.05) | -0.08 (0.04)* | -0.01(0.04) |

[1] OR = ovulation rate; IE = implanted embryos; TB = total born; ES = embryo survival; FS = foetal survival; PS= prenatal survival; L:LP line; *significant difference (α=0.05).

Regarding the crosses involving lines V and LP, significant differences showed that when V line was used as a dam the cross had a high embryo survival but the post-implantation losses were high. According to the differences obtained, the LH cross would be preferable to the reciprocal because of its relevant advantage on OR. Thus, in these crosses the H line should be used as dam line. However, in the crosses LV and VL seems better to use the V line as the dam line, as we have commented before. The superiority of a cross with respect to its reciprocal suggests the existence of maternal genetic effects for the traits showing this difference.

Table 5. 5 shows the differences between direct genetic effects of the lines according to the Dickerson model. In general, there were not significant differences in direct genetic effects between H, LP and V lines, and the differences actually estimated between the three lines were always lower than 7 % of the respective means.The results were very different for the comparison between the A line and the others, and important differences were observed, unfavourable for the A line, almost in all traits. For direct genetic effects on TB, Baselga *et al.* (2003) and Orengo *et al.* (2003) found significant differences in favour of the V line. The last authors also found significant differences between H and A line, having a favourable effect of the H line in this trait.

**Table 5. 5**Contrasts (standard errors) for direct genetic effects (D) between lines.

| | **OR**[1] | **IE**[1] | **TB**[1] | **ES**[1] | **FS**[1] | **PS**[1] |
|---|---|---|---|---|---|---|
| D:A-H | -1.38(0.86) | -0.71(1.03) | -1.45(1.16) | 0.04(0.06) | -0.06(0.06) | -0.02(0.07) |
| D:A-L | -2.01(0.78)* | -1.75(1.18) | -2.13(1.06)* | 0.01(0.06) | -0.07(0.06) | -0.05(0.06) |
| D:A-V | -1.29(0.73) | -0.60(1.01) | -1.88(0.99) | 0.05(0.05) | -0.09(0.05) | -0.04(0.06) |
| D:H-V | 0.09(0.64) | 0.11(0.97) | -0.43(0.82) | 0.01(0.05) | -0.03(0.04) | -0.02(0.04) |
| D:L-H | 0.64(0.80) | 1.03(0.80) | 0.68(1.03) | 0.03(0.06) | 0.02(0.05) | 0.03(0.06) |
| D:L-V | 0.73(0.66) | 1.15(1.06) | 0.25(0.83) | 0.04(0.05) | -0.02(0.04) | 0.01(0.05) |

[1] OR = ovulation rate; IE = implanted embryos; TB = total born; ES = embryo survival; FS = foetal survival; PS = prenatal survival; L:LP line; * significant difference (α=0.05).

Regarding the maternal genetic effects (Table 5. 6), no significant effects were observed for any trait except for OR. This was negative for the LP line with respect to any of the other lines. The A line had a favourable maternal effect compared with the other lines. In crossing experiments, Baselga *et al.*

(2003) and Orengo *et al*. (2003) did not obtain any significant maternal genetic effect between the lines A, V and H for TB.

**Table 5. 6**Contrasts (standard errors) for maternal genetic effects (M) between lines.

| | **OR**[1] | **IE**[1] | **TB**[1] | **ES**[1] | **FS**[1] | **PS**[1] |
|---|---|---|---|---|---|---|
| M:A-H | 0.24(0.46) | 0.32(0.49) | 0.25(0.60) | 0.02(0.03) | 0.00(0.03) | 0.01(0.03) |
| M:A-L | 1.25*(0.46) | 1.07(0.70) | 0.47(0.60) | 0.01(0.03) | -0.01(0.03) | -0.00(0.03) |
| M:A-V | 0.34(0.45) | -0.08(0.67) | 0.76(0.58) | -0.01(0.03) | 0.06(0.03) | 0.03(0.03) |
| M:H-V | 0.10(0.42) | -0.34(0.64) | 0.51(0.55) | -0.03(0.03) | 0.05(0.03) | 0.03(0.03) |
| M:L-H | -1.01*(0.41) | -0.65(0.62) | -0.22(0.56) | 0.01(0.03) | 0.01(0.03) | 0.01(0.03) |
| M:L-V | -0.91*(0.44) | -0.99(0.66) | 0.29(0.54) | -0.02(0.03) | 0.07*(0.03) | 0.03(0.03) |

[1] OR=ovulation rate; IE=implanted embryos; TB=total born; ES = embryo survival; FS = foetal survival; PS= prenatal survival; L:LP line; * significant difference (α=0.05).

The results indicate that the range of variation of the estimated heterosis across the different crosses is relatively wide and includes negative values for all traits (Table 5. 7). Expressed as % of the means of the lines involved, they ranged between 7.6 and -2.42 % for OR, 11 and -3.46 % for IE, 13.06 and -15.41 % for TB. Great negative values were observed only in the case of the cross between LP and V lines. Favourable individual heterosis with significant values were observed between A and H lines. Under the theory of dominance, the heterosis is a function of the genetic distance (gene frequency differences) between the lines involved in the cross and the dominance parameter (Falconer and Mackay, 1996).

The estimates of the direct heterosis for all traits between the lines H and V were non significant and must be noted that the H line was created with participation of the V line (Cifre *et al*., 1998). The same happened for the LP line; this line also had influence of the V line in its foundation, but the individual heterosis between them was negative and significant for some of the analysed traits. It is difficult to find a common explanation for these, apparently, contradictory results. There are very few estimates of crossbreeding parameters for litter size components in the literature. Regarding survival traits, the crosses LH and LV for FS and PS showed significant estimates. In these cases the estimates were around 7-10% for FS and 8-11 % for PS, always significant and negative.

**Table 5. 7**Estimates (standard errors) of the heterosis (H) for the crossbred groups.

| | **OR**[1] | **IE**[1] | **TB**[1] | **ES**[1] | **FS**[1] | **PS**[1] |
|---|---|---|---|---|---|---|
| H:AH | 1.16(0.50)* | 1.46(0.60) * | 1.44(0.62)* | 0.03(0.04) | 0.01(0.04) | 0.03(0.04) |
| H:AL | 0.27(0.49) | 0.58(0.61) | -0.29(0.61) | 0.03(0.04) | -0.06(0.04) | -0.03(0.04) |
| H:AV | 0.70(0.41) | 0.92(0.51) | 0.74(0.52) | 0.03(0.03) | -0.01(0.03) | 0.01(0.03) |
| H:HV | 0.88(0.49) | 0.98(0.55) | 0.43(0.59) | 0.02(0.03) | -0.01(0.04) | -0.00(0.03) |
| H:LH | 0.58(0.43) | 0.36(0.51) | -0.54(0.54) | -0.01(0.03) | -0.06(0.03)* | -0.06(0.03)* |
| H:LV | -0.37(0.38) | -0.46(0.47) | -1.70(0.40)* | -0.01(0.03) | -0.08(0.02)* | -0.08(0.02)* |

[1] OR=ovulation rate; IE=implanted embryos; TB=total born; ES = embryo survival; FS = fetal survival; PS= prenatal survival; L:LP line; * significant difference (α=0.05).

In rabbits, Hulot and Matheron (1979) and Brun *et al*. (1992) detected positive and significant heterosis for ovulation rate and prenatal survival. Baselga *et al*. (2003) found a significant heterosis in AH and AV but with smaller values than the ones obtained in our study whereas the very low heterosis values found in HV were not significant. In another study involving a cross between the INRA 2066 and the V lines to form the INRA 2666 line, Brun and Baselga (2005) found significant heterosis for TB and NBA with similar values to the one obtained by the cross between A and H lines. In mice, Falconer and Roberts (1960) and Boshier (1968) performed studies to know the results of crossing inbred lines. All results supported the conclusion that ovulation rate shows little, if any, heterosis. The last author found a considerable degree of heterosis for fetal survival. Only the inbreeding experiment reported by McCarthy (1967) showed evidence of dominance in genes affecting this trait. In swine, King and Young (1957) suggested a considerable degree of dominance for genes affecting ovulation rate, whereas Galvin *et al*. (1993) did not observe individual heterosis for ovulation rate and embryo survival. But they concluded that crossbred sows had a very high level of fetal survival compared with the purebred females.

## 5.5 Conclusions

Important differences in components of litter size have been observed in simple crosses of different maternal lines, some of them between reciprocal crosses, especially for ovulation rate.The lines were very similar in direct genetic effects with the only exception of one of them that was clearly inferior. The maternal genetic effects were mainly important for ovulation rate, in agreement with the results for the reciprocal effects. The heterosis was positive for ovulation rate and implanted embryos in most of the crossbred groups and more commonly negligible for foetal and prenatal survival. All these effects seem more important for ovulation rate than for the embryonic, foetal or prenatal survival.

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Chapter 6

# Reproduction traits in a diallel cross of four maternal lines of rabbits

## 6.1 Abstract

A complete diallel cross involving four maternal lines of rabbits, that produce sixteen genetic groups, was carried out to evaluate the genetic groups and to estimate the crossbreeding genetic parameters of litter size (total born (**TB**), number born alive (**NBA**) and number weaned(**NW**)) and kindling interval (**KI**). The experiment was designed involving the A, V, H and LP lines, all of them selected for litter size at weaning. A total of 34,546 parities, distributed between the sixteen genetic types, were analysed. The pedigree had 7,111 animals. The sixteen genetic groups were distributed in four Spanish farms but only one genetic group (V line) was present in all farms in order to connect records among these farms and to be used as reference group in the comparison with the other genetic groups. An animal model was used to estimate components of variance using a REML procedure. Finally, the differences between lines, direct and maternal genetic effects, and individual heterosis were estimated according to Dickerson model after solving the appropriate animal model conditioned on the REML variance components.

The obtained differences between the performances of the lines were of low magnitude and not significant for litter size traits. The LP line showed the shortest KI, having relevant differences with respect to the other lines (5.49, 5.39 and 2.39 days respect to the lines A, V and H). Also, H line had a shorter KI than A and V lines, with differences of 3.10 and 2.99 days with respect to these lines that did not show significant differences between them. These differences reflected the differences between direct and maternal genetic effects.

The crossbred does showed a higher reproductive level than the V line which is commonly used in many Spanish farms, as a maternal line to produce crossbred does. The differences between the average of all crosses and line V were found to be significant and seemed to be important, being 0.46 for TB, 0.56 for NBA, 0.75 for NW and -2.21 days for KI, indicatingthe importance ofthecross between lines for obtaining a high litter size with a short KI.

In this study, the differences between reciprocal crosses for litter size were of low magnitude and non-significant. This result is an indication that the maternal effects are not important.

Only, the LP line presented a higher direct genetic effect than the V line that was significant for NBA. The other lines did not show significant differences in direct and maternal genetic effects for TB, NBA and NW but there were some significant differences for KI which ranged from 1.54 to 6.85 d in direct effects and from 0.63 to 3.38 d for maternal effects.

A positive and, in some cases, relevant heterosis was found in this study. The largest heterosis was for TB in the HV cross (1.05 rabbits), followed by the AH (0.74 rabbits), AV (0.57 rabbits) and BH (0.55 rabbits) crosses. For NBA, significant heterosis was found in HV (1.11 rabbits) and AV (0.49 rabbits) and for NW in AV (0.90 rabbits), LH (0.70 rabbits) and LV (0.58 rabbits). Favourable and significant heterosis for KI was found in AV (-2.54 d) and LV (-1.03 d) crosses, whereas it was unfavourable in AL (1.91 d) and in LH (3.60 d).

**Key words:** diallel cross, heterosis, kindling interval, litter size, maternal lines, rabbits.

## 6.2 Introduction

Litter size is important in the selection programs of rabbit maternal lines because its improvement allows producing kits to a lower cost (Armero and Blasco (1992). In general, the heritability estimates of litter size are lower than

0.15 and its repeatability lower than 0.25 (Mantovani *et al.*, 2008; Piles *et al.,* 2006). Hence, the expected response to direct selection for this trait is low, but the estimated responses have been even lower than expected. The genetic trends estimated by mixed model methodology ranged from 0.05 to 0.13 kits born alive or weaned per litter and generation (Estany *et al.,* 1989; Rochambeau *et al.,* 1994 and Gómez *et al.,* 1996). Using the same methodology, García and Baselga (2002a, b) found that the genetic trend was 0.175 and 0.09 weaned kits per generation in lines A and V, respectively.

It is important to note that selection in finite populations has cumulated effects increasing inbreeding (Verrier *et al.*, 1990; Wray *et al.*, 1990; Wray and Thompson, 1990), augmenting the variation between lines and changing the gene frequency between populations. Therefore, crossbreeding is one of the tools for exploiting genetic variation between populations. Its main purpose is to produce superior crosses, taking profit of the direct and maternal genetic effects of the lines, the heterosis between them (Long, 1980; Johnson, 1981), their complementaryand the break of the accumulated inbreeding during the selection of the lines (Baselga, 2004). Previous selection and inbreeding can have an effect on the degree of heterosis by changing the gene frequency of the genes affecting the trait because the heterosis is positively related to the genetic distance between the parental lines (Brun and Baselga, 2005;Xu, 2003).

In most studies in rabbits direct heterosis had a positive effect on total born and number born alive whereas it was always positive for litter size at weaning (Khalil *et al*., 1995; Brun *et al*., 1998; Baselga *et al*., 2003; Orengo *et al*., 2003; Youssef *et al*., 2008). Negative values were obtained in few studies for total born and number born alive (Khalil *et al*., 1995; Iraqi *et al*., 2006). Many studies did not show maternal heterosis for litter size traits (Baselga *et al*., 2003 and Iraqi *et al*., 2006) whereas other authors have found positive values of this parameter (Nofal *et al*., 2005; Khalil *et al*., 2005).

The aims of the present experiment were to evaluate the genetic types in a diallel cross among four maternal lines of rabbits that had been selected for litter size at weaning, in order to determine which the best ones are, and to provide estimates of the crossbreeding parameters of the traits associated with the reproductive performance of the does.

## 6.3 Materials and Methods

### *6.3.1 Animals and Management*

A diallel cross involving four maternal lines of rabbits (A, V, H, and LP, selected for litter size at weaning and described previously by Ragab and Baselga, 2011) was carried out. Their current generation of selection is 41st, 37th, 20th and 7th, respectively. Data were collected from January 2009 to October 2011.

The experimental work was carried out in 4 Spanish farms with a total of 2,260 cages available for breeding animals. The total number of data set was 34,546 parities from 7,111 does distributed between the different farms. The farms were located in León (farm 1, 8,984 parities), Castellón (farm 2, 7,844 parties), Tarragona (farm 3, 9,837 parities) and Valencia, Universidad Politécnica de Valencia (UPV) (farm 4, 7,881 parities). The genetic groups involved in the experiment were the 4 purebred lines (AA, VV, HH and LL) and the 12 single crosses: AV, VA. AH, HA, AL, LA, VH, HV, VL, LV, HL and LH. Notice that first letter of the cross names corresponds to the sire line name involved in the cross whereasthe second one corresponds to the dam line name, and L is used to identify the LP line.

Farms 1 and 2 raised all the crossbreds and the purebred V animals; the farm 3 raised females of the groups VV and HH, and the farm 4 housed VV, AA and LL animals. The line V was present in all the farms to connect data between farms and to be used as a common reference line. The number of parities in every genetic group was 2,293 for AA, 1,272 for AL, 1,110 for AH, 1,304 for AV, 963 for HA, 4,610 for HH, 1,418 for HL, 1,332 for HV, 1,114 for LA, 1,252 for LH, 2,772 for LL, 1,482 for LV, 1,250 for VA, 1,124 for VH, 1,078 for VL and 10,172 for VV.

Animal management slightly differed across farms. In farm1 and 2 does were grouped into a single batch mated every 42 days, while in farms 3 and 4 does were grouped into 6 batches and weekly matings were practised. In all farms, the first mating was around 18 weeks of age for males and females. Natural mating was used in farm 3 and 4 while artificial insemination was conducted in farms 1 and 2 by using semen from a paternal line (10-20x$10^6$ spermatozoa per dose) with a prior injection of gonadotropin (20 U.I.) to induce the ovulation. The semen was collected 16 hours before insemination. The does were served 10-12 days post-kindling and a pregnancy test was carried out by abdominal palpation on day 12 after mating. Litters were reared by their dams during 28 days and no fostering was practised.

Does were fed *ad libitum* on a standard commercial pelleted diet and they were under a constant photoperiod of 16:8 h.

### 6.3.2 Traits and Statistical analyses

The considered prolificacy traits were total born (**TB**), number born alive (**NBA**) and litter size at weaning (**NW**, 28 days). Additionally, a fertility trait was studied, which was defined by the kindling interval (number of days between two consecutives parities, **KI**).

All the prolificacy traits were analysed using the following univariate mixed model:

$$Y_{ijkl} = GFYS_i + PS_j + a_k + p_k + e_{ijkl} \qquad \text{(Model 1)}$$

Where $Y_{ijkl}$ is the record $l$ of the trait being analysed (TB, BA or NBA), corresponding to the $k$ doe which was in the physiological status $j$ and belongs to the genetic group-farm-year-season combination $i$; $GFYS_i$ is the fixed effect of the genetic group-farm-year-season combination $i$ (317 levels); $PS_j$ is the fixed effect of the doe physiological state $j$ (5 levels depending on the parity order and lactation state at mating, where 1 is for nulliparous does, 2 (4) for primiparous lactating (non-lactating), and 3 (5) for multiparous lactating (non-lactating)); $a_k$ is the random effect of the additive value of the doe $k$, related across animals through the numerator relationship matrix, **A** ( 8,205 animals); $p_k$is the random permanent environmental plus non-additive genetic effects of the doe $k$; and $e_{ijkl}$ is random the residual of the model.

The analysis of KI was carried out by using the following univariate model:

$$Y_{ijkl} = GFYS_i + PO_j + a_k + p_k + e_{ijkl} \qquad \text{(Model 2)}$$

Where $Y_{ijkl}$ is the $l$ record corresponding to the $k$ doe which was in parity order $j$ and belongs to the genetic group-farm-year-season combination $i$, $PO_j$is the parity order and the other components of the model were defined as in model 1.

In a previous step, the variance components for the models were estimated using the remlf90 program (Misztal *et al*., 2002). Given the previously estimated variance components, models were solved using the blupf90 program (Misztal *et al*., 2002) to get the estimates of the differences between all the genetic groups and the VV group, as well as the (co)variance matrix between these estimates. From these contrasts and their variance covariance structure the differences between direct and maternal genetic effects of the lines as well as the individual heterosis were estimated by generalized least squares according to the Dickerson's model (Dickerson, 1969). Chi-squared tests, assuming as true the provided residual variances, were conducted, setting the type I error at 0.05.

## 6.4 Results and Discussions

Table 6. 1 shows raw means and standard deviations for the traits measured in this study. Notice the high prolificacy showed by all the genetic groups. The values of TB, NBA and NW traits are in agreement or they are slightly higher than other values previously reported by other authors in rabbit maternal lines (García and Baselga 2002a, b; Costa *et al*., 2004; Theilgaard *et al*., 2007; Al-Saef *et al*., 2008; Sánchez *et al*., 2008; Ragab and Baselga, 2011).

**Table 6. 1** Descriptive statistics of the experimental data.

| | Number | Mean | Minimum | Maximum | SD |
|---|---|---|---|---|---|
| Total born | 34,546 | 10.54 | 1 | 24 | 3.33 |
| Number born alive | 34,546 | 9.79 | 0 | 21 | 3.43 |
| Number weaned | 34,546 | 7.97 | 0 | 20 | 3.42 |
| Kindling interval | 27,449 | 49.91 | 36 | 169 | 13.7 |

SD: standard deviation

The heritability estimates were rather low and tended to decrease from birth to weaning. The estimated heritability (repeatability in brackets) was 0.07 (0.18), 0.06 (0.18), 0.03 (0.12) and 0.03 (0.08) for TB, NBA, NW and KI, respectively. There is a wide range of heritability estimates of litter size traits reported in previous studies; however, some authors have found similar estimates to the ones here presented (Ferraz and Eler, 1996; Baselga *et al*., 2003; Piles *et al*., 2006; Mantovani *et al*., 2008). It must be noted that in our case we deal with purebred and crossbred populations, and these estimated heritabilities must be understood as a balance of the additive gene effects in different genetic frameworks, such as the genetic types considered in this work.

The differences between the performances of the genetic groups corresponding to the purebred does can be observed in Table 6. 2. These contrasts involve direct and maternal genetic effects. We did not find significant differences between the lines for all the litter size traits, but significant differences were found for KI. The LP line had the shortest KI, whereas the largest KI were observed in A and V lines. Differences of around 5.4 days (10.82% of the mean) were observed between these two lines and the LP line. The KI differences of A and V with respect to H animals were around 3 days (6.01%).

It seems that lines show similar performances in prolificacy traits. This could be understood as consequence of a successful selection process for litter size at weaning, particularly for the A line. The lack of differences between lines agree with previous results reported by Ragab and Baselga (2011) and it is contrary to results obtained by Orengo *et al*. (2003) who showed superiority of line V over line A. Baselga *et al*. (2003) also confirmed this superiority.

However, the last authors did not find significant differences between line H and lines V and A. Sánchez *et al*. (2008) found that the average differences between LP and V lines for TB, NBA and NW favour the V line but with low probabilities (0.20) of these contrasts of being greater than 0.Similar results were found by Ragab and Baselga (2011).

**Table 6. 2**Contrasts (standard error) between the genetic groups of the lines for litter size traits (rabbits) and kindling interval (days).

| | Total born | Born alive | Number weaned | Kindling interval |
|---|---|---|---|---|
| AA-LL | -0.37(0.29) | -0.38(0.29) | -0.21(0.24) | 5.49(0.75)* |
| AA-HH | -0.16(0.37) | -0.20(0.37) | -0.06(0.31) | 3.10(1.15)* |
| AA-VV | -0.16(0.27) | -0.16(0.27) | 0.23(0.22) | 0.10(0.75) |
| LL-HH | 0.21(0.37) | 0.19(0.37) | 0.15(0.31) | -2.39(1.10)* |
| LL-VV | 0.21(0.26) | 0.22(0.26) | 0.44(0.22) | -5.39(0.66)* |
| HH-VV | 0.00(0.26) | 0.05(0.26) | 0.29(0.22) | -2.99(0.88)* |

L:LP line; *: significant difference at α = 0.05

In general, favourable and important differences for all traits were found between crossbred does and V line (Table 6. 3)which is the most widely used line to produce crossbred does in Spain and many countries (Garrue *et al.,* 2004). These differences were found to be positive and significant for TB (AH, HV and LH), for NBA (AH, HV, AV and LH) and for NW (AH, AL, AV, LH and LV).

**Table 6. 3**Contrasts (standard error) between crossbred groups[1] and V line for litter size traits (rabbits) and kindling interval (days).

| | Total born | Born alive | Number weaned | Kindling interval |
|---|---|---|---|---|
| AH-VV | 0.65(0.30)* | 0.66(0.32)* | 0.68(0.28)* | -2.83(0.99)* |
| AL-VV | -0.21(0.30) | 0.02(0.31) | 0.53(0.27)* | -0.88(0.77) |
| AV-VV | 0.44(0.24) | 0.51(0.26)* | 0.96(0.23)* | -2.31(0.65)* |
| HV-VV | 1.04(0.31)* | 1.10(0.33)* | 0.49(0.29) | -2.84(0.91)* |
| LH-VV | 0.65(0.29)* | 0.79(0.31)* | 1.06(0.27)* | -0.66(0.74) |
| LV-VV | 0.12(0.24) | 0.31(0.26) | 0.81(0.23)* | -3.80(0.61)* |
| All-VV | 0.46(0.23)* | 0.56(0.24)* | 0.75(0.21)* | -2.21(0.60)* |

[1]. One cross and its reciprocal are considered together;All-VV: the contrast between all crossbred and V line; *: L:LP line; significant difference at α = 0.05.

The magnitude of the differences was particularly important for the case of NW, which is the selection criterion of these lines. This trait has a genetic determinism close to the one of litter size at marketing and reflects, indirectly, the milk yield and maternal ability of the does (Ragab and Baselga, 2011). The magnitude of the differences for NW between the different crosses and VV animals ranged between 6.14 % and 13.30 % of the mean of the trait.

Regarding KI, most crosses had significantly shorter KI than V line and the differences were important. The difference between the average of all crossbred groups and the V line was significant and favourable to crossbred groups for all traits, indicatingthe importance ofthecrossbreeding for having a high litter size with a short KI.

An indicator of the relevance in using a particular line either as sire or dam is got by checking the contrast between a particular cross and it's reciprocal. Reciprocal effects reflect differences in gene frequencies between two lines in the presence of additive maternal and (or) dominance maternal effects (Eisen *et al.*, 1983). Regarding litter size traits, no reciprocal effects were found (Table 6. 4) between all genetic groups. For the case of KI some important differences between reciprocal crosses were observed. This was the case for the crosses involving the lines A and LP, A and H, LP and V, and V and H lines. This indicates that the best performance could be achieved under a particular reciprocal cross, being that an indicator of maternal effects, as it will be discussed later.

**Table 6. 4**Contrasts (standard error) between reciprocal crosses for litter size traits (rabbits) and kindling interval (days).

| | **Total born** | **Born alive** | **Number weaned** | **Kindling interval** |
|---|---|---|---|---|
| AL-LA | 0.44(0.28) | 0.27(0.31) | 0.22(0.28) | 3.78(0.78)* |
| AH-HA | 0.02(0.37) | -0.15(0.40) | 0.01(0.36) | 4.25(1.54)* |
| AV-VA | -0.09(0.26) | -0.16(0.28) | -0.26(0.26) | 0.38(0.76) |
| LH-HL | 0.10(0.35) | 0.25(0.37) | 0.10(0.33) | 0.62(0.84) |
| LV-VL | 0.39(0.28) | 0.24(0.31) | 0.19(0.28) | 4.11(0.68)* |
| HV-VH | 0.18(0.36) | 0.32(0.39) | 0.57(0.36) | 2.99(1.30)* |

L:LP line; *: significant difference at α = 0.05.

Table 6. 5 shows the estimates of the differences between the lines on direct and maternal genetic effects and the heterosis of the crosses. In general, no significant differences were found for direct and maternal genetic effects for litter size. The only significant difference was observed between LP and V lines for NBA in direct genetic effect, favouring the L line. The general absence of detected differences is an indicator of the similarity between lines for the

direct genetic effects and maternal abilities. The differences between maternal genetic effects were lower in magnitude compared to those between direct genetic effects. Eisen *et al*. (1983) discussed two possible explanations for this: i) maternal genetic effects on litter size may be small compared to direct genetic effects; ii), the covariance between direct and maternal genetic effects for litter size may not be large enough to shift gene frequencies at loci primarily affecting maternal performance.

The differences between lines for direct genetic effects on KI were significant and favouring LP, H and V lines with respect to the A line. Regarding maternal effects, the differences between lines could be also said to be significant; particularly the A line showed a favourable effect with respect to H, V and LP lines, whereas the differences between LP and V lines on this parameter favoured LP line.

**Table 6. 5**Contrast (standard error) for direct (D) and maternal (M) genetic effects.

| | Total born | Born alive | Number weaned | Kindling interval |
|---|---|---|---|---|
| D:AA-HH | -0.09(0.42) | 0.02(0.43) | -0.18(0.37) | 5.11(1.35)* |
| D:AA-LL | -0.30(0.35) | -0.52(0.36) | -0.25(0.31) | 6.85(0.93)* |
| D:AA-VV | 0.02(0.33) | 0.17(0.34) | 0.27(0.29) | 3.56(0.94)* |
| D:HH-VV | 0.11(0.33) | 0.16(0.35) | 0.45(0.31) | -1.54(1.11) |
| D:LL-HH | 0.21(0.41) | 0.55(0.42) | 0.07(0.37) | -1.74(1.22) |
| D:LL-VV | 0.32(0.32) | 0.70(0.34)* | 0.51(0.29) | -3.28(0.83)* |
| M:AA-HH | -0.07(0.25) | 0.07(0.27) | 0.15(0.24) | -1.86(0.80)* |
| M:AA-LL | -0.08(0.21) | 0.06(0.23) | 0.04(0.20) | -1.23(0.59)* |
| M:AA-VV | -0.19(0.20) | -0.05(0.22) | -0.03(0.20) | -3.38(0.59)* |
| M:HH-VV | -0.12(0.24) | -0.12(0.26) | -0.18(0.24) | -1.51(0.76) |
| M:LL-HH | 0.01(0.25) | 0.01(0.27) | 0.11(0.24) | -0.63(0.69) |
| M:LL-VV | -0.11(0.21) | -0.11(0.23) | -0.07(0.21) | -2.15(0.55)* |

L:LP line; $^*$: significant difference at α = 0.05.

Baselga *et al*. (2003) found significant higher differences on direct genetic effects for V line on TB, NBA and KI with respect to A line, but non-significant differences were found in the contrasts regarding direct genetic effect involving the H line. These authors did not find any significant difference regarding maternal genetic effects. In other workinvolving A and V lines, it was found that V line showed a significantly higher direct effect than A line for TB and NBA but not for NW and KI (Orengo *et al*., 2003).

For some of the analysed traits, some crosses showed significant direct heterotic effects, but the magnitude of this parameter widely varied (Table 6. 6). These favourable effects on litter size traits indicate the importance of the use of crossbreeding to take advantage of the heterotic effects on these traits.

The largest positive response for TB was found for the cross between H and V lines followed by those between A and H, A and V and between lines LP and H. Regarding NBA, the crosses between H and V and A and V were those showing the strongest heterosis. Finally for NW the crosses involving A and V, LP and H and LP and V were those showing the significant effects. The magnitudes of the heterosis seem to be relevant for all traits, particularly for NW. The AV and LV groups had favourable and significant direct heterosis for KI while AL and LH had a larger KI than their parental lines.

Only two works were carried out involving some of the lines presented in this study. Orengo *et al*. (2003) found that heterosis effect was not significantly different from 0 between A and V lines for TB, NBA, NW and KI. On the contrary, Baselga *et al*. (2003) found significant heterosis between the same lines for TB (0.48) and NBA (0.55) but this effect was not significant for KI (-1.59). Other authors found positive and important direct heterosis in different crosses, some of them involving the V line: V x A2066 (Brun and Baselga, 2005), V x Baladi Red (Youssef *et al.,* 2008), Egyptian Gabali x NZW (Khalil and Afifi, 2000), NZW x CAL (Nofal *et al.,* 1996) and A1077 x A2066 (Brun and Saleil 1994).

AV showed significant differences for litter size traits which could be due to the large selection history of the two lines involved in the cross and their genetic distance. The heterosis is defined according to the differences in gene frequency as well as directional dominance, and selection history or genetic drift to which the involved lines might be subject to (Horstgen-Schwark *et al*. 1984). The same explanation can be given for the large heterosis values presented by the AH group, although we found it was significant only for TB.

**Table 6. 6**Estimates (standard errors) of the heterosis (H) for crossed genetic group.

| | Total born | Born alive | Number weaned | Kindling interval |
|---|---|---|---|---|
| H:AL | -0.19(0.23) | -0.29(0.26) | 0.22(0.24) | 1.91(0.69)* |
| H:AH | 0.74(0.28)* | 0.58(0.31) | 0.44(0.27) | -0.56(0.92) |
| H:AV | 0.57(0.21)* | 0.49(0.23)* | 0.90(0.21)* | -2.54(0.61)* |
| H:LH | 0.55(0.28)* | 0.48(0.30) | 0.70(0.27)* | 3.60(0.77)* |
| H:LV | 0.00(0.22) | 0.01(0.24) | 0.58(0.22)* | -1.03(0.57)* |
| H:HV | 1.05(0.33)* | 1.11(0.35)* | 0.41(0.30) | -0.82(0.94) |

L:LP line; *: significant difference at $\alpha = 0.05$.

## 6.5 Conclusions

Important differences between performances in reproductive traits have been observed in simple crosses of different maternal lines. These differences can be related to differences between the lines in direct and maternal genetic effects, but particularly to the direct heterosis effects of the crosses.

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## Chapter 7

# Functional longevity in a diallel cross of four maternal lines of rabbits.

## 7.1 Abstract

The objective of this study was to evaluate four maternal lines of rabbits and the corresponding crossbred does from a complete diallel cross regarding functional longevity, estimating its crossbreeding parameters. The lines involved were the A, V, H and LP that were used to produce sixteen genetic groups (the four lines and twelve single crosses). The lines considered have been selected for litter size at weaning, some of them for a long time.

Functional longevity was defined, in this study, as the number of days between the first positive palpation and the death or culling of the doe for reasons other than production; it represents the ability to delay involuntary culling. A total of 7,211 doe longevity records were obtained from January 2009 to October 2011. The sixteen groups were distributed in four Spanish farms but only one group (line V) was present in all farms to connect the data among farms and to be used as the reference line in the comparison with the other groups. The data were analysed with the Survival kit 6.0 using a Cox proportional hazard model (Cox, 1972) of fixed effects. The model incorporated time-dependent factors, such as group-farm-year-season, number of kits born alive, group-order of positive palpation and physiological status of the female. Finally, the differences between groups, direct and maternal genetic effects of the lines and individual heterosis were estimated according to Dickerson (1969).

Does from lines A, H and V had a similar risk to die or to be culled and they were more sensitive than those from line LP. Line LP had the lowest associated hazard with important differences at later ages and the risks to be replaced were 0.39, 0.49 and 0.53 times the replacement risk of lines A, H and V. We did not find significant differences between all crossbred groups and line V except when comparing V line tothe cross between A and H lines favouringV line (1.30 higher risk of replacement for AxH animals).

The difference between a cross and its reciprocal, generally, was not significant except between VH and HV, favourable to HV (0.72 of relative risk of replacement) and between LH and HL, in favour of HL (0.76 of relative risk). Line V had the highest associated risk due to the direct genetic effects and these differences were significant with the lines H (1.40 of relative risk) and LP (1.43 of relative risk). The differences in maternal genetic effects were small and found to be not significant except between lines H and V in favour of V line (0.75 of relative risk).

The estimated heterosis effects do not follow, always, the same direction but they showed, in some cases, the importance of the crosses between specialized lines to produce crossbred does for intensive meat rabbit production. Thus, it was shown that at the early productive cycles, the risk associated to purebreds is higher than the risk of crossbreds, when the cost of the does has not been recovered yet. The contrary happened at late productive cycles (fifth cycle or more), when the cost of the does was recovered.

**Keywords**: maternal lines, diallel cross, longevity, survival analysis, heterosis.

## 7.2 Introduction

Functional longevity in rabbits has been defined as the time in days between the first positive palpation of a doe and death or culling due to non-productive reasons (Sánchez *et al.,* 2004). Improvement of productive life of does is needed because the replacement rate is very high (120%, Ramón *et al*.,

1996) being this a consequence of the high rate of death and sickness especially during the first production cycle, when the cost of the does has not been yet recovered. Other consequence of the high replacement rates is that the proportion of young does in production is high and these does are more difficult to handle than the older ones and they show significantly less production (Sánchez *et al.,* 2004). Another issue related to the high replacement rate is the increased risk of health problems as a consequence of the higher proportion of animals coming into the farm periodically. Moreover, longevity is related to diseases resistance and animal welfare, which both are topics of current concern to the public opinion.

There are a number of issues involves in the genetic improvement of longevity: it has low heritability (Piles *et al.,* 2006b; Sánchez *et al.,* 2008) and it is recorded late in the animal life when they die or are culled. Sánchez *et al.* (2008) considered, as selection criterion for founding a new line, the number of parturitions that a female had, applying very high intensities of selection. This founding procedure was proved to be successful (Sánchez *et al.,* 2008) because this line had a very similar productive level compared to lines selected for a long time for prolificacy (Ragab and Baselga, 2011), butbetter survival. Other experiment carried out in France, consisted on performing divergent selection for functional longevity in the INRA 1077 rabbit line (Garreau *et al.,* 2008). The authors found a significant difference in longevity between the two lines (0.92 inseminations (39 days)). Culling and mortality rates were lower in the line selected for increasing longevity than in that selected to reduce longevity.

Functional longevity has a low heritability, as it has been said before, but variation between genetic groups has been observed (Piles *et al.,* 2006b; Sánchez *et al.,* 2008). So, it would be possible to exploit the genetic variation between the lines to optimize the crosses between them. Crossbreeding has been documented in pigs, beef cattle, and sheep to have a substantial impact on traits directly related to fertility and health and indirectly to longevity.

To our knowledge, very few works have been carried out to study genetic variability of rabbit longevity among breeds, lines and crossbreds. In a study, conducted by Piles *et al.* (2006a), a complete diallel cross, involving three maternal lines of rabbits (A, V, Prat), was performed to estimate crossbreeding parameters for functional longevity. They found favourable and significant heterosis between lines A and Prat, and between the lines V and Prat. In a different work by Lukefahr and Hamilton (2000) involving Californian (CAL), New Zealand White (NZW) and CAL x NZW does, it was observed a higher longevity for NZW than for CAL; crossbred does behaved similarly to NZW.

The objective of this work was to evaluate functional longevity of crossbred and purebred does from a complete diallel cross of four maternal lines of rabbits and the corresponding crossbreeding parameters.

## 7.3 Materials and Methods

### *7.3.1 Animals and Management*

Four maternal lines of rabbits were available in this study for conducting a diallel cross that produced sixteen genetic groups. The lines were A, V, H and LP, all of them selected for litter size at weaning, as described previously by Ragab and Baselga (2011). Their current generation of selection was the 41st, 37th, 20th and 7th, respectively. Data were collected from January 2009 to October 2011.

The animals in this study were allocated to four Spanish farms. The total data were 7,211 longevity records, with the following distribution: 1,822 in León (farm 1), 1,987 in Castellón (farm 2), 1,612 in Tarragona (farm 3) and finally 1,790 in the farm of the Universidad Politécnica de Valencia (UPV) (farm 4). The genetic groups involved in the experiment were the corresponding to the four lines, AA, VV, HH and LL, and the twelve single crosses, AV, VA, AH, HA, AL, LA, VH, HV, VL, LV, HL and LH, where the first letter refers to the sire line, and the second to the dam line of the group, and L is used to identify the LP line.

All the crossbreds and VV animals were bred in farms 1 and 2; does from VV and HH were bred in the farm 3, and VV, AA and LL animals were bred in farm

4. Thus the V line was present in all the farms, which allowed connecting data among farms, allowing the correction for environmental effects and the comparison of genetic groups between farms.

Management was slightly different across farms. In farm 1 and 2 (after October 2010, in farm 2) does were grouped in a single batch mated every 42 days, while in farms 2 (before October 2010), 3 and 4 does were grouped into 6 batches and mating were weekly practiced. In all farms, the first mating of was around 18 weeks of age, for males and females. Natural mating was used in farms 3 and 4 whereas artificial insemination was conducted in farms 1 and 2. In farm 1 and 2, does were inseminated with semen from a paternal line (10-20x$10^6$ spermatozoa per dose). The does were served 10-12 days post-kindling and a pregnancy test was carried out by abdominal palpation on day 12 after mating. Litters were reared by their dams for about 28 days. Does were fed *ad libitum* on a standard commercial pelleted diet and they were under a constant photoperiod of 16:8 h. As a general management practice, does were never culled due to productive reasons, i.e. low prolificacy or fertility was never a reason for culling except when there were also signs of sickness.

The complete data set included records of sixteen genetic groups, involving 7,211 does, 38.61% of them having a censored longevity record because they were removed before the end of their productive lives or the experiment finished before their death date. Table 7. 1 presents the maximum, minimum and average length of productive life for censored and uncensored records.

**Table 7. 1**Minimum, maximum and average productive life for censored and uncensored records.

| | **Censored records**<br>2784 (38.61%) | **Uncensored records**<br>4427 (61.39%) |
|---|---|---|
| Minimum time (d) | 5 | 3 |
| Maximum time (d) | 895 | 873 |
| Average time (d) | 334.43 | 196.82 |

### *7.3.2 Statistical analyses*

The Cox model of proportional risk was used to analyse the productive life of the does, following the next equation for the hazard:

$$h_m(t|\boldsymbol{x}_m(t)) = h_0(t) * exp\{GFYS_i(t) + NBA_j(t) + GPPO_k(t) + PS_l(t)\}$$

where, the hazard $(h_m(t|\boldsymbol{x}_m(t))$ of the doe $m$ at time t) affected by the covariates indicated in the vector $\boldsymbol{x}_m(t)$ is the product of a base line hazard at time t, $h_0(t)$, and the exponential effect of the components of $\boldsymbol{x}_m(t)$. $GFYS_i(t)$ is the effect of genetic group-farm-year-season combination of the doe $m$at time $t$; this is a time-dependent factor with 145 levels. The changes of the levels occurred at fixed calendar dates, leading to approximately 90 days seasons. $NBA_j(t)$ is the effect of the number born alive class $j$ at time $t$. This was also a time-dependent effect with 9 classes defined as follows: nulliparous, 0, 1 to 2, 3 to 4, 5 to 6, 7 to 8, 9 to 10, 11 to 12, and >12 born alive; for this factor levels changed at every parity. $GPPO_k(t)$ is the effect of the combination $k$ between the genetic group and positive palpation order at time $t$; this was also fitted as a time-dependent factor with 80 levels. It allows taking into account the possible effect of the interaction between the genotype and the parity order. $PS_l(t)$is the time-dependent effect of the physiological status $l$ of the doe at time $t$. This factor reflects the combination between the reproductive status of the females (pregnant, non-pregnant, unknown) and its lactational status (lactating or non-lactating).

Data analysis was conducted using the Survival Kit 6.0 (Ducrocq *et al.,* 2010). The model was solved to get the estimates of the differences between all the genetic groups and the VV group, as well as the (co)variance matrix between these estimates. From these contrasts and their variance-covariance structure the differences between direct and maternal genetic effects of the lines, as well as the individual heterosis, were estimated by generalized least squares according to the Dickerson's model (Dickerson, 1969). The significance of the estimated contrasts and heterosis were assessed setting the first type error at α=0.05.

## 7.4 Results and Discussion

The contrasts for the log hazard between the four maternal lines, globally and for the different productive cycles are presented in Table 7. 2. Line LP showed the highest capacity to overcome the risk factors which can lead to death or culling. It showed hazard ratios with respect to A, H and V lines of 0.77 (exp (-0.26)), 0.82 and 0.78 respectively being the log-hazard ratio significant for the cases involving A and V lines. These figures mean that the risks of death or culling of females from A, H and V lines were 1.29, 1.22 and 1.28 times the risk of LP does. No overall significant differences were found between A, H and V lines. The fact that the differences favoured LP line was expected because this line was founded by selecting females from commercial farms that showed an extremely long productive life which was measured as a function of the number of parities (Sánchez *et al.,* 2008) while for the other lines nor the foundation neither the selection process relied on longevity criteria (Ragab and Baselga, 2011). In a study comparing LP and V lines for longevity, Sánchez *et al.* (2008) reported that the mean of the relative risk between LP and V lines was 0.80 (exp (-0.22)), which indicated that it was 1.24 times more likely for a V doe to leave the herd than for an LP doe.

**Table 7. 2**Contrasts (standard errors) between lines for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | GR | P1 | P2 | P3 | P4 | ≥P5 |
|---|---|---|---|---|---|---|
| AA-HH | 0.06(0.16) | 0.61(0.24)* | 0.40(0.25) | -0.04(0.25) | -0.38(0.22) | -0.31(0.26) |
| AA-LL | 0.26(0.11)* | 0.29(0.19) | 0.05(0.20) | 0.18(0.22) | -0.07(0.18) | 0.83(0.27)* |
| AA-VV | 0.00( 0.10) | 0.20(0.15) | 0.21(0.17) | -0.10(0.18) | -0.38(0.15)* | 0.09(0.21) |
| HH-VV | -0.05(0.13) | -0.41(0.20)* | -0.19(0.21) | -0.06(0.20) | 0.00(0.18) | 0.40(0.18)* |
| LL-HH | -0.20(0.16) | 0.33(0.25) | 0.35(0.25) | -0.22(0.26) | -0.31(0.23) | -1.15(0.26)* |
| LL-VV | -0.25(0.10)* | -0.08(0.17) | 0.16(0.17) | -0.28(0.19) | -0.31(0.15)* | -0.75(0.21)* |

L:LP line; *: significant difference at α = 0.05.

Performing the same set of contrasts within positive palpation order (number of productive cycle), it was observed that at the first cycle A and V does had 1.84 and 1.51, respectively, more risk to leave the herd than H line does. During the second and third cycle, no significant differences were observed between lines. The apparition of global significant differences between A and V lines with respect to LP animals was due to the fact that at the latest cycles significant differences between lines were observed. In the fourth cycle there was 1.36 times more risk for a V female to be dead or be culled than for a LP doe, whereas in the fifth parity this ratio was 2.14. In the fifth cycle the risk ratios between A, V and H lines with respect to LP were significant, showing the values of 2.3, 2.14 and 3.15, respectively. It makes sense that the differences in survival ability between all the lines and the LP females are essentially set at late parities since the selection criteria of this line during its foundation was based on survival ability until very late ages, i. e. more than 28 parities.

In the fifth cycle, it was also observed a better survival rate for the V line than for the H line, compensating the higher risk associated to the V line at early cycles.

With regard to the general differences between crossbred does (considering together each cross and its reciprocal, Table 7. 3) and line V, we did not find any significant differences between the crossbred groups and line V, except for the cross between A and H lines, which was favourable to line V. Analysing the same differences by productive cycle, significant differences were found at the first cycle and during cycles equal or higher to the 5th. At the first cycle, the groups HL and LH, and LV and VL showed favourable and significant differences with respect to V line for the associated risk. However the does of the group HA and AH had higher risks to leave the herd than does of the V line at the first cycle (1.36). Moreover, in general, no significant differences were found at third and fourth cycles, except a significant difference in favour of crosses LH and HL at the third cycle. At cycle orders ≥ 5, the crossbreds had higher associated hazards than V line. The differences were relevant and the relative risk ranged from 1.32 to 2.34, this is a clear indication of the fact that crossbred doesat the beginning of the reproductive career seemed to show some advantages over line V,but they failed to keep this situation at final stages of the productive life.

**Table 7. 3**Contrasts (standard errors) between crossbred groups[1] and V line for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | **GR** | **P1** | **P2** | **P3** | **P4** | **≥P5** |
|---|---|---|---|---|---|---|
| AH-VV | 0.26(0.08)* | 0.31(0.13)* | -0.06(0.16) | -0.04(0.16) | 0.24(0.16) | 0.85(0.16)* |
| AL-VV | 0.03(0.09) | 0.04(0.14) | -0.15(0.17) | -0.16(0.17) | 0.00(0.15) | 0.42(0.16)* |
| AV-VV | -0.07(0.09) | -0.21(0.14) | -0.10(0.15) | -0.21(0.17) | -0.14(0.15) | 0.28(0.16) |
| HV-VV | 0.01(0.09) | -0.07(0.14) | -0.12(0.15) | -0.33(0.17) | -0.02(0.15) | 0.60(0.15)* |
| LH-VV | -0.07(0.08) | -0.38(0.14)* | -0.08(0.14) | -0.34(0.17)* | -0.10(0.15) | 0.57(0.14)* |
| LV-VV | -0.04(0.09) | -0.45(0.15)* | -0.29(0.16) | 0.03(0.17) | -0.01(0.16) | 0.54(0.15)* |
| All *vs* VV | 0.02(0.06) | -0.13(0.09) | -0.13(0.10) | -0.18(0.11) | 0.00(0.10) | 0.54(0.10)* |

[1]. One cross and its reciprocal are considered together; L:LP line; *: significant difference at α = 0.05.

Sánchez *et al.* (2004) and Piles *et al.*(2006b) reported that late productive cycles are always associated with high risk and low survival. At the initial productive cycles, when the associated risk was still low, purebred does may have a lower survival probability than the crossbred does. In the former groups, more sick or dead does would leave the flock, but those does remaining would show lower risks in the future. However, the crossbred does had at the initial cycles a low elimination rate and after some cycles the possibility of appearing sick or dead does would increase.Moreover, the crossbred does had a high production level which with time must increase the risk of culling or death.Anyway, it should be noted that the increased risk associated with crossbred does began at the fifth cycle, when the cost of the does has been recovered. Moreover, Rosell (2003) reported that around 50 % of the dead and culled does are in one of the first three kindlings, so it is important to use the crossbred does in commercial production.

Table 7. 4 shows the differences between the estimates of log hazard associated with reciprocal crosses, to give a first indication of the magnitude of maternal effects involved in the crosses. The only significant contrasts were found between VH and HV and between LH and HL.For the first case, when the V line was used as a dam line the hazard ratio associated to VH was reduced to 0.72, but when the line H was the dam in the cross between H and LP lines, the risk of culling or death was 1.31 (exp (0.27)) times higher than in the reciprocal cross. The significant differences between HV and VH crosses are

consequence of differences between them during the first cycle while for the case of LH and HL crosses the differences are established late in the doe's life.

For the contrast between AH and HA crosses although not overall significant differences were detected, during the first cycle the risk was higher for the cross HA (1.95) but at latest cycles the opposite occurred and the higher risk was for the reciprocal (1.89).

**Table 7. 4**Contrasts (standard errors) between reciprocal crosses for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | GR | P1 | P2 | P3 | P4 | ≥P5 |
|---|---|---|---|---|---|---|
| AH-HA | 0.04(0.13) | -0.67(0.22)* | 0.14(0.28) | -0.29(0.28) | 0.34(0.27) | 0.64(0.26)* |
| AL-LA | -0.02(0.14) | 0.05(0.23) | -0.36(0.29) | 0.18(0.29) | -0.06(0.26) | 0.08(0.26) |
| AV-VA | -0.05(0.15) | 0.31(0.25) | -0.02(0.27) | -0.21(0.29) | -0.42(0.26) | 0.11(0.28) |
| HV-VH | -0.32(0.15)* | -1.20(0.23)* | -0.13(0.26) | -0.31(0.29) | -0.01(0.25) | 0.03(0.24) |
| LH-HL | 0.27(0.13)* | 0.06(0.23) | 0.34(0.24) | 0.20(0.29) | 0.10(0.26) | 0.65(0.23)* |
| LV-VL | -0.17(0.15) | -0.19(0.26) | -0.17(0.28) | -0.18(0.29) | -0.19(0.27) | -0.13(0.24) |

L:LP line; $^*$: significant difference at $\alpha = 0.05$.

Differences in direct genetic effects between lines are presented in Table 7. 5. There are two results that deserve attention. The first one is that line V had the highest associated risk and its differences were significant with respect to the lines H and LP. In the case of the H line, the difference to the V line are due to a high and important risk associated to V line at the first productive cycle, but in the case of the LP line, the differences were established during the fourth and later productive cycles. The second important result is that the direct effect of the LP line had the lowest associated hazard, especially at cycles≥ 5. Its risk, at these cycles, was only, 0.39, 0.49 and 0.53 times the risk for A, H and V lines, respectively. Also, from Table 7. 5 it can be concluded that no significant differences were observed between A and V lines, either globally or at any cycle.

In another study (Piles *et al.*, 2006a) where lines A, V and Prat were evaluated, it was not found any significant differences between direct genetic effects of A and V lines. However the relative risk between both lines in that study was higher than in our work. In that study significant differences on direct genetic effects between A and Prat lines were found. In our study, for some cases, differences between direct genetic effects generated at certain cycles were compensated with differences of opposite sign generated at other cycles, being not possible to observe overall significant differences. This is what happened between A and H lines and between LP and H lines.

**Table 7. 5**Contrasts (standard error) for direct genetic effects (D) between lines for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | **GR** | **P1** | **P2** | **P3** | **P4** | **≥P5** |
|---|---|---|---|---|---|---|
| D:A-H | 0.20(0.19) | 0.62(0.29)* | 0.50(0.31) | -0.08(0.32) | -0.31(0.29) | 0.21(0.32) |
| D:A-L | 0.21(0.15) | 0.22(0.25) | -0.14(0.28) | 0.14(0.30) | -0.10(0.26) | 0.94(0.32)* |
| D:A-V | -0.15(0.14) | -0.22(0.23) | 0.08(0.25) | -0.36(0.27) | -0.56(0.24) | 0.31(0.28) |
| D:H-V | -0.34(0.16)* | -0.84(0.26)* | -0.42(0.28) | -0.28(0.29) | -0.25(0.26) | 0.10(0.25) |
| D:L-H | -0.02(0.19) | 0.40(0.30) | 0.64(0.31)* | -0.22(0.33) | -0.21(0.29) | -0.72(0.31)* |
| D:L-V | -0.36(0.14)* | -0.44(0.24) | 0.22(0.26) | -0.50(0.28) | -0.47(0.24)* | -0.62(0.27)* |

L:LP line; *: significant difference at α = 0.05.

The observed differences in global risk between lines regarding maternal genetic effects were small and in general they were not significant, except between lines H and V in favour of V line (Table 7. 6). But along the life of the animals some significant differences were observed. During the first productive cycle the difference in the maternal genetic effect between A, H and LP lines and the V line was found to be significant and favourable to the last one. Late in the life of the animals, it was observed a negative effect of the maternal effect associated to the H line, compared to the maternal effects of the lines A and LP. The estimated differences in maternal effects approximately match the observed differences between any cross and its reciprocal as it is shown in Table 7. 4. Piles *et al* (2006a) found a similar value for the difference of maternal effects between A and V lines, but this difference was not significant.

**Table 7. 6**Contrast (standard error) for maternal (M) line effects for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | GR | P1 | P2 | P3 | P4 | ≥P5 |
|---|---|---|---|---|---|---|
| M:A-H | -0.14( 0.10) | -0.01(0.16) | -0.10(0.19) | 0.04(0.20) | -0.07(0.18) | -0.53(0.18)* |
| M:A-L | 0.05( 0.10) | 0.07(0.16) | 0.19(0.20) | 0.05(0.20) | 0.03(0.18) | -0.10(0.18) |
| M:A-V | 0.15( 0.10) | 0.42(0.17)* | 0.12(0.19) | 0.27(0.20) | 0.19(0.18) | -0.23(0.18) |
| M:H-V | 0.29( 0.10)* | 0.43(0.16)* | 0.23(0.19) | 0.22(0.20) | 0.25(0.18) | 0.30(0.17) |
| M:L-H | -0.19( 0.10) | -0.07(0.16) | -0.29(0.18) | -0.01(0.20) | -0.09(0.18) | -0.42(0.17)* |
| M:L-V | 0.11( 0.10) | 0.36(0.17)* | -0.06(0.19) | 0.22(0.20) | 0.16(0.18) | -0.13(0.17) |

L:LP line; $^*$: significant difference at α = 0.05.

The estimated values for the individual heterosis depended on the lines involved in the cross (Table 7. 7). In general, the heterosis for the global log hazard has not been significant, except for the cross AH, which had an unfavourable value (positive risk associated to the cross). However when different lifetime periods are considered, it is important to note that, late cycles are always associated with significant and relevant, but unfavourable, heterosis effects. Contrarily, at early ages some favourable effects were observed. The difference in the sign of estimates at early and late ages could be explained arguing the higher elimination rate at early cycles in purebred groups and the high productive levels of crossbred does. Piles *et al.* (2006a) found favourable heterosis in crosses between A, Prat and V line but it was only significant between A and Prat lines.

**Table 7. 7**Estimates (standard error) for heterosis (H) for the global log hazard (GR) and for the log hazard associated with the positive palpation order (P1, P2, P3, P4, ≥P5).

| | GR | P1 | P2 | P3 | P4 | ≥P5 |
|---|---|---|---|---|---|---|
| H:AH | 0.28(0.12)* | 0.35(0.17)* | -0.06(0.19) | 0.03(0.19) | 0.45(0.18)* | 0.62(0.19)* |
| H:AL | 0.16(0.12) | -0.02(0.17) | -0.34(0.19) | 0.04(0.20) | 0.34(0.18) | 0.76( 0.20)* |
| H:AV | -0.08( 0.10) | -0.31(0.15)* | -0.21(0.16) | -0.16(0.18) | 0.05(0.16) | 0.23(0.18) |
| H:HV | 0.04(0.11) | 0.14(0.16) | -0.02(0.17) | -0.30(0.18) | 0.00(0.16) | 0.42(0.16)* |
| H:LH | 0.10(0.12) | -0.13(0.18) | -0.07(0.18) | -0.16(0.20) | 0.05(0.18) | 0.76(0.18)* |
| H:LV | 0.09( 0.10) | -0.41(0.16)* | -0.38(0.17)* | 0.17(0.18) | 0.14(0.16) | 0.91(0.17)* |

L:LP line; $^*$: significant difference at α = 0.05.

## 7.5 Conclusions

The criterion of foundation of LP lines marked its difference with the other lines in favour of LP line. It seemed that the heterosis did not have a great effect on functional longevity. The differences between genetic groups were mainly produced at the beginning and at the end of the productive life.

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Chapter 8

# General Discussion

The objective of a genetic improvement program is the development and diffusion of genetic material to the farmers at the lowest cost. Rabbit meat production follows a pyramidal structure in which the peak of the pyramid is represented by animals of the lines selected by maternal and paternal traits located in the nucleus of selection. The maternal lines are commonly selected within line and used to produce crossbred does from simple crosses between them. The Animal Breeding Unit of the Institute for Animal Science and Technology (Polytechnic University of Valencia, Spain) started back in 1976 a rabbit breeding program aiming at developing and selecting lines of interest for rabbit meat production. The program has included the development of four maternal lines, the A, V, H and LP lines. The first two were founded early, after the beginning of the program, and the other two later, being the LP line the most recent one. The criterion of foundation has been different for each line and all of them have been selected from their foundation for litter size at weaning. The set of the four maternal lines gives the opportunity of studying the consequences of the foundation criteria on the performance of the lines and how their selection affects the comparison between them along the generations. Finally, it is possible and necessary to assess the value of the lines for rabbit meat production, analysing the current performance of the lines themselves and their crosses. The study of the crosses allows the estimation of the corresponding crossbreeding parameters.

The selection criteria and procedures used for founding the lines are of paramount importance because the initial performance and peculiar features of the lines can depend on them.The responses obtained by subsequent selection will be accumulated over the values achieved at foundation. The results obtained in this thesis (Chapter 3) show that V, H and LP lines were superior to A line for all litter size traits (Total born, number born alive, litter size at weaning and at marketing), between this last line and the other lines there were important differences at foundation time. Productive criterions, such as, maternal aptitude of crossbred does, hyperprolificacy and length of high productive life were used for the foundation of the V, H and LP lines, while A line was created by mating does and bucks of the New Zealand White breed that primarily maintained the standards of the breed, assuming that if the founders pertained to a reputed breed for rabbit meat production they would have competitive performances, clearly this was not the case.The LP line had advantage in litter size traits over the V line. The former was founded by selecting does at commercial farms excelling because of their high longevity but being also above the mean in prolificacy (Sánchez *et al*., 2008). This procedure of foundation led to the LP line to have high starting performances and a peculiar robustness to face challenging circumstances that sometimes appears, as outbreaks of diseases, bad management practices, heat stress and others. The robustness of the LP line was proved in one experiment carried out to compare the V and the LP lines. In this experiment, a change in the mating management for lines LP and V increased the period of restricted feeding by 2 weeks between weaning and the next parity. This restriction affected more to the line V than to the line LP (Theilgaard *et al*., 2007; Sánchez *et al*., 2008) because the line LP showed a better management of the body reserves. There were not found significant differences between H and V lines for litter size, probably because the H line was founded following a criterion of hyperprolificacy with contribution of the V line (Cifre *et al*., 1998).

The foundation may continue affecting the performance of the lines despite of the selection for long time of some of them. This was shown when lines A, H and V were compared during the period from March 1997 to August 1998 (after different number of generations of selection). During this period the lines were still affected by the foundation criterions, i.e. line A showed the lowest performances but the differences to the other lines were reduced. From September 2007 to February 2009, after a long period of selection of the A and V lines, these lines and the LP line were compared. At this period the differences at the foundation between them were highly reduced, being the comparisons, in general, non-significant for litter size traits. The A line was recovered from the negative effect of its foundation criterion. This study also shows the importance of the interaction between line and environment (farm-year-season) to explain the differences between the lines and the consequent necessity of including this effect into the models used for the analysis of the production traits.The importance of this interaction was clearly observed in two cases. Firstly, the spread of the enterocolitis affected a long period comprised during the comparison between the lines A and H. The consequence of this disease was an increase in the post-weaning mortality, reducing the number of rabbits marketed. However, the sensitivity to enterocolitis differed among the lines, being line A that most strongly affected. Secondly, the change in mating management of LP and V lines which was commented above.

Previous selection and inbreeding as well as genetic drift can have an effect on the gene frequency of the genes affecting a trait. Inbreeding is the result of mating between relatives and implies an increase of homozygosis within the populations (Falconer and Mackay, 1996). Inbreeding negatively affects the means of the traits and lead to an increased risk in a breeding program in terms of the variance of genetic gain (Meuwissen, 1991). It is known that time and selection, natural or artificial, can diminish the depressive effect of the inbreeding, due to a reduction of the frequency of unfavorable alleles, genetic purging, and the consequent reduction of the genetic load (Templeton and Read, 1984; Lacy and Ballou, 1998). So, the next objective of the thesis was to study the change of the inbreeding and its effects on litter size traits along the generations of selection of the lines (Chapter 4). Assessing the change of inbreeding over time allows the computation of the effective population size of the lines when selection and some management practices, adopted to reduce the rate of inbreeding increase, are applied. The study of the inbreeding effect, using the data of A, V and H lines allows differentiate its effects as a function of the time of its accumulation. Moreover, it allows showing the special difficulties inherent to the data of programs of selectionto analyse the effect of inbreeding. It was shown, that the effect of selection, which leads to increase the inbreeding by reducing the effective population size (Wray and Thompson, 1990), was counterbalanced by the opposite effects of avoiding matings between close relatives and the similarity of contributions to the next generation of the animals that actually contribute.To study the effects of the inbreeding on litter size traits, as a function of the time of its accumulation, the inbreeding of each animal was split in three components named old, intermediate and new inbreeding. This partition can separate efficiently the effects of each component because the correlation between the three is negligible or very low. It was found that the old inbreeding had a positive, important and significant effect on all litter size traits while the new inbreeding had a negative effect that our data cannot prove as significantly different from zero. However, the difference of the effect of the old inbreeding to the intermediate and new inbreeding was significant for almost all the comparisons. The previous results show how the common presence of selection and inbreeding along long periods of time has beneficial effects. This situation allows the purging of unfavourable alleles for the traits selected or for the traits closely related to them. This action was observed in plants by Byers and Waller (1991), in mice by Hinrichs *et al*. (2007) and in Irish Holstein-Friesians byParland *et al*. (2009). So, to study the inbreeding depression, it is better to consider only the last generations of selection, not the accumulated inbreeding, especially if the inbreeding is studied in lines with a long history of selection.

The inbreeding depression estimated in most of the previous studies was in populations with a short number of generations. Thus, these values should be compared with the effects, here estimated, for the new inbreeding. For example Ferraz *et al*. (1991) and Moura *et al*. (2000), in rabbits, have previously reported negative effects of inbreeding on prolificacy traits that are more important than the ones obtained in this study for the new inbreeding. It seems that this effect is actually lower in our lines. Effects of the inbreeding of the magnitude estimated by Ferraz *et al*. (1991) and Moura *et al*. (2000) would had masked the response to selection in the lines V and A, response that has been proved (García and Baselga, 2002a, b). Similarly, when crossbred does between different generations of line A and V were compared (Costa *et al*., 2004; Quevedo *et al*., 2005), the differences were, only, a little higher than expected from the intra-line response to selection which is an indicator of low inbreeding depression.

Crossbreeding is a widely accepted and recommended practice in commercial rabbit production. It is used to capitalize on heterosis and complementarity, the superiority of crossbred individuals over the average of their purebred counterparts (Baselga, 2004). The heterosis, in the absence of epistasis, is determined by the dominance parameter of the genes affecting the traits and by the difference in frequencies of these genes between the lines (Falconer and Mackay, 1996). The selection causes changes in the gene frequency at loci having direct genetic effects on traits, changes that can also occur at random by genetic drift in populations of small size. The results of a large diallel cross experiment between the four maternal lines are presented in chapters 4, 5 and 6, where litter size components (Chapter 5), litter size (Chapter 6) and functional longevity (Chapter 7) of the lines and their simple crosses are studied. The experiment was carried out in four farms. The line V was present in all the farms to connect the data.

The differences between performances of the lines were important for total born from the point of view of rabbit production (chapter 5). These differences were partially due to an outbreak of colitis in one of the farms (where lines A, V and LP were raised) that was active during the second part of the period of study. The sensitivity to this pathology was different among lines, being the A line that most strongly affected. This disease provoked a decrease in the fetal survival, a reduction in the number of total born as well as an increase in the mortality at birth. These data were part of a large set of data used in the analysis of litter size traits (Chapter 6) and, consequently, its importance on the comparison of the lines was small.The differences between lines were mainly due to differences in direct effects more than to differences in maternal effects. It is speculated that changes in maternal effects due to selection are lower than in direct effects. Eisen *et al*. (1984) discussed this question, they pointed in one hand that genes influencing maternal effects on litter size may have smaller effects and, in the other that the covariance between direct and maternal genetic effects may not be particularly large, so that loci affecting primarily maternal influences had not shifted much in gene frequency. However, some differences in maternal effects can be due to differences in the original background of the lines and to the genetic drift and, in fact, some significant differences have been detected between reciprocal crosses, these differences are related to different maternal effects across lines.

In general, there were not significant heterosis for ovulation rate, implanted embryos and total born, except for the case of the AH cross which exhibited the highest percentage of direct heterosis for all mentioned traits. A and H lines are probably the mostgenetically distant populations, because the line V had a relevant contribution in the process of foundation of bothH and LP lines H. In fact, all crossbred groups showed some degree of positive heterosis except LV animals that was unexpectedly negative for all traits and significant for total born, fetal and prenatal survival. Falconer and Robert (1960) reported that ovulation rate did not show directional dominance and it was not affected by inbreeding. Boshier (1968) support the conclusion that ovulation rate shows a little, if any, heterosis. However, in rabbits Hulot and Matheron (1979) and Brun *et al*. (1992) detected positive and significant heterosis for ovulation rate and prenatal survival.The standard errors in our experiment only allow to accept as significant estimated heterosis equal or higher to 6% of the mean of ovulation rate and to 9% or higher of the mean of implanted embryos.

Regarding litter size, chapter 5, not significant differences were observed and it matches well the differences observed in chapter 3 from the comparison between the lines at the interval from September 2007 to February 2009. Regarding kindling interval, the line comparison was favourable for the LP line and unfavourable for the lines A and V, result that could be in agreement with the high capability of the LP line to recover from stress and to manage its body ressources (Theilgaard *et al.*, 2007). Crossbred does showed a higher reproductive level and shorter kindling interval than the V line indicatingthe general importance ofcrossbreeding. In this study, the differences between reciprocal crosses for litter size were of low magnitude and always non-significant. This result is an indicator that the maternal effects have lowrelevance. The estaimated heterosis effect for litter size traits match to the expectations for reproduction traits associated to fitness. The heterosis estimated were positive and, in some cases, highly relevant. The largest heterosis was observed for total born in the HV cross (1.05 rabbits), followed by the AH (0.74 rabbits), AV (0.57 rabbits) and LH (0.55 rabbits) crosses. For number born alive significant heterosis was found in HV (1.11 rabbits) and AV (0.49 rabbits) and for number weaned in AV (0.90 rabbits), LH (0.70 rabbits) and LV (0.58 rabbits). Favourable and significant heterosis for kindling interval was found in AV (-2.54 d) and LV (-1.03 d) crosses, whereas it was unfavourable for AL, 1.91 d and for LH, 3.60 d. Summarizing the importance of the crossbreeding parameters in the determination of differences in performances of the crossbreds, we can conclude that for litter size traits the heterosis was the most relevantfactor;however for kindling interval all the crossbreeding parameters: direct, maternal and heterosis effects, significantlycontributed to explain the differences between lines.

The replacement rate in rabbit meat production farms is very high (120%), (Ramón and Rafel, 2002).Therefore, doe longevity is of great economic importance because: (1) the higher the number of litters produced by a doe, the greater the opportunity to spread doe costs over a longer period of time;(2) increased longevity tends to extend the parity distribution at the expense of lower parity orders, increasing rabbit per doe per year through an increased litter size and a reduced replacement rate; (3) the high replacement rate, when the replacement animals are bought outside, implies a higher risk of health problems; (4) it is related with disease resistance and animal welfare, subjects of current concern.

Functional longevity of the lines and their crossbreds is analysed in Chapter 7. Lines A, H and V had a similar ability to avoid risks and they were more sensitive than line LP. Line LP had the lowest associated hazard with important differences at later ages. The superiority of LP line was expected because this line was founded by selecting females from commercial farms that showed an extremely long productive life, which was measured as a function of the number of parities (Sánchez *et al.*, 2008).Comparing the average of all crossbred groups to the V line few significant differences were found for the whole reproductive career of the does but, at the first reproductive cycles, the crossbreds used to have lower risks than the V line and the contrary situation occurred at later cycles. Sánchez *et al.* (2004) and Piles *et al.* (2006b), working with pure lines, reported that late productive cycles are always associated with high risk and low survival. At the initial productive cycles, when the associated risk was still low, does of the pure lines may have a lower survival probability than crossbred does. However, crossbred does that had at the initial cycles a low elimination rate, after some cycles of high performance the possibility of appearing sick or dead does would increase. The difference between a cross and its reciprocal, generally, was not significant except between VH and HV, being favourable to HV, and between LH and HL, in favour of HL. That indicates that line H has unfavourable maternal effects on functional longevity.

The differences between lines in direct genetic effects were in the same direction that the differences commented between lines, in favour of LP line, that had a very similar effect to the H line and significantly superior to the V line. This line did not show significant differences with line A in direct genetic effects.Piles *et al.* (2006a) did not find significant differences between direct genetic effects between the A and V lines, but significant differences were found between the lines A and Prat. In our study, in some cases, differences between direct genetic effects generated at certain cycles were compensated with differences of opposite sign generated at other cycles, being not possible to observe overall significant differences. This is what happened between A and H and between LP and H.

The pattern of the heterosis effects associated to the crosses is very similar to the pattern already commented for the crossbreds respect to the V line. Thus the higher values of heterosis were related to the first and late cycles of the crossbred does. The crossbred does had high survival ability at the initial cycles, when the risk of elimination or death is high and the cost of the does has not recovered yet, and at the late cycles the hazard clearly increased.Consequently, it should be noted that the increased risk associated with crossbred does began at the fifth cycle, when the cost of the does has been recovered. Rosell (2003) reported that around 50 % of the dead and culled does are in one of the first three kindlings, so it is interesting to use the crossbred does in a commercial production to reduce early replacements.

A final question, of practical interest, is to analyse if there are some crosses that could be specially recommended to be used in commercial production.To discuss this question it is necessary to take into account that in our study no fostering of kit has been carried out between the does after kindling, but this practice is common among the farmers to reduce the losses during the lactation.In general, the crosseswith participation of line H are the ones with the best reproductive performances. The HL crosswas the best forthe set of analysed traits, especially for litter size at weaning which is important due to its closed genetic correlation with litter size at marketing. Also, HL had a higher survivalthan LH in global survival and especially at the late productive cycles. The HV cross can be one of the most interest if fostering is applied. This cross had higher ovulation rate, total born and number born alive than the other crossbred groups. Moreover, HV is better than VH because the latter had higherrisk than the former, especially at the first productive cycles. The cross between A and V lines is the most widely used in Spain; this cross did not show important differences for total born with respect to V line, whereas it had a great number of born alive and weaned kits which reflectsits high maternal capacity. Another interesting cross is AH which showed higher reproductive performances than most of crossbred groups and V line. However, this cross had higher risk of death or culling than the other genetic groups, at early and late reproductive cycles, result that precludes its recommendation for farms with medium or low management level.

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Chapter 9

# Final conclusions

1. Reproductive performances of the four maternal lines (A, V, H and LP) were high and they appeared to be *a priori* competitive lines to produce commercial crossbred does.
2. Important differences were detected between the lines at their origin, which can be explained based on their foundation criteria.
3. Strong agreement has been found between the observed differences of the lines at fixed times and the expected differences that are computed with the models that take into account the selection. This agreement, especially for litter size traits, is considered as an indicator of the appropriateness of these models.
4. The effects of selection to increase inbreeding can be counterbalanced by the opposite effects of avoiding matings between close relatives and the similarity of contributions to the next generation of the animals that actually contribute.
5. The effects of old, intermediate and new inbreeding on litter size traits change from positive, for old inbreeding, to negative for new inbreeding and values in between them for intermediate inbreeding, due to the fact that the purging of unfavourable genes is favoured, along the generations, by the inbreeding, natural and artificial selection, acting jointly.
6. Important differences between performances in litter size and litter size components have been observed in simple crosses of different maternal lines.

7. The direct heterosis was positive with relevant values for litter size traits, especially litter size at weaning.
8. The criterion of foundation of LP line marked its differences for functional longevity with the other lines in favour of LP line.
9. It seemed that the heterosis did not have a great effect on functional longevity but, in general, the crossbred groups showed a high longevity at early reproductive cycles which is important in the field of rabbit production.
10. It seems that HxLP, HxV and AxV or VxA are the crossbred does to be specially recommended for commercial production.The cross AxH could be recommended for farms where the longevity is not a problem.